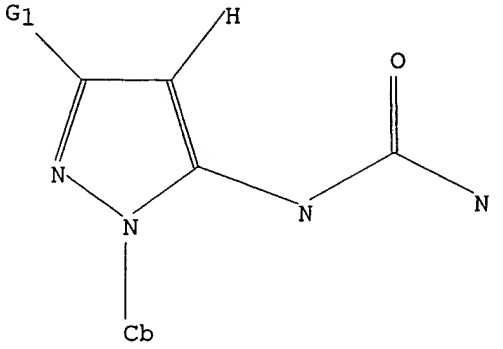
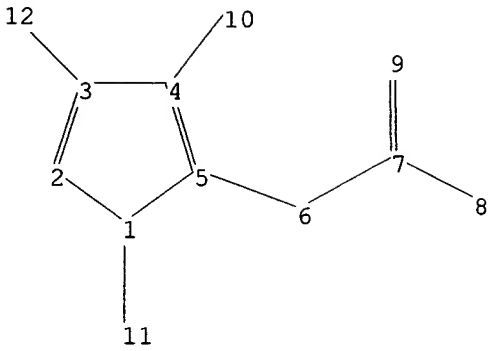
Uploading C:\Program Files\Stnexp\Queries\09776935g.str





chain nodes :
6 7 8 9 10 11 12
ring nodes :
1 2 3 4 5
chain bonds :
1-11 3-12 4-10 5-6 6-7 7-8 7-9
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 2-3 3-12 5-6 6-7 7-8 7-9
exact bonds :
1-11 3-4 4-5 4-10
isolated ring systems :
containing 1 :

G1:Cb,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:Atom 12:CLASS
Generic attributes :
11:
Saturation : Unsaturated

Element Count :
Node 11: Limited
C,C6-14

L12 STRUCTURE UPLOADED

=> s l12
SAMPLE SEARCH INITIATED 16:01:54 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 308 TO ITERATE

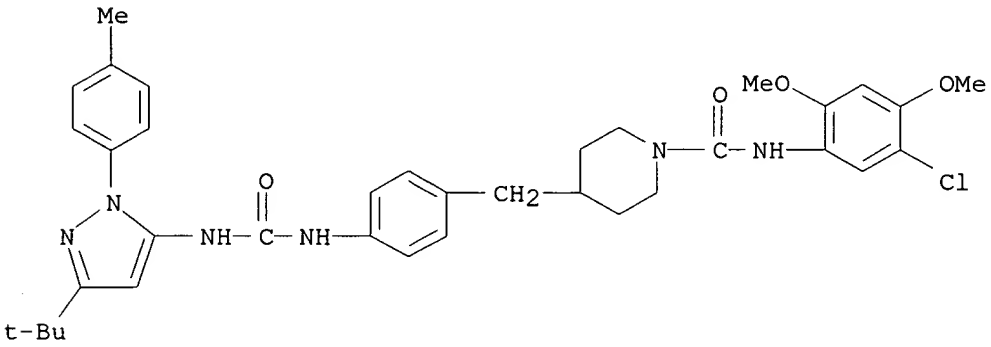
100.0% PROCESSED 308 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 5108 TO 7212
PROJECTED ANSWERS: 1114 TO 2206

L13 50 SEA SSS SAM L12

=> d scan

L13 50 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN 1-Piperidinecarboxamide, N-(5-chloro-2,4-dimethoxyphenyl)-4-[[4-[[[[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]phenyl]methyl]- (9CI)
MF C36 H43 Cl N6 O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s l12 full
FULL SEARCH INITIATED 16:02:10 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 5410 TO ITERATE

100.0% PROCESSED 5410 ITERATIONS 1505 ANSWERS
SEARCH TIME: 00.00.01

L14 1505 SEA SSS FUL L12

```
=> s l14
L15         180 L14

=> s l15 and (rheumatoid or crohn? or osteoarthritis or osteoporosis or osteroporosis or asthma
or septic or sepsis or ibd or (inflammatory bowel disease) or p38 or (graft (3w) host))
L16         131 L15 AND (RHEUMATOID OR CROHN? OR OSTEOARTHRITIS OR OSTEOPOROSIS
                OR OSTEROPOROSIS OR ASTHMA OR SEPTIC OR SEPSIS OR IBD OR (INFLAM
                MATORY BOWEL DISEASE) OR P38 OR (GRAFT (3W) HOST))

=> dup rem l16
PROCESSING COMPLETED FOR L16
L17          119 DUP REM L16 (12 DUPLICATES REMOVED)

=> d 1-119 bib abs

L17  ANSWER 1 OF 119  HCAPLUS  COPYRIGHT 2005 ACS on STN DUPLICATE 1
AN   2005:1004352  HCAPLUS
DN   143:279459
TI   Compositions and methods for preventing and treating skin and hair
     conditions
IN   David, Nathaniel E.
PA   VVII NewCo 2003, Inc., USA
SO   U.S. Pat. Appl. Publ., 16 pp.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 3
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   US 2005203111        A1    20050915    US 2004-799867         20040312
     WO 2005091891        A2    20051006    WO 2005-US6300         20050225
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
             SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
PRAI US 2004-799540       A     20040311
     US 2004-799867       A     20040312
     US 2004-810391       A     20040326
AB   The present invention discloses compns. and methods for the prevention and
     treatment of skin and hair diseases, such as, for example, alopecia,
     psoriasis, and keloids.  In one embodiment, the present invention
     discloses a method for preventing and treating hair loss by applying
     locally to a region lacking hair a p38.alpha. MAP kinase
     inhibitor.  The p38.alpha. MAP kinase inhibitor is preferably
     formulated as a gel, ointment, spray or solution that can be applied
     topically, transdermally, or s.c. to the targeted region.  The p38
     inhibitor is especially RDP-58, AMG-548, BIRB-796, CNI-1493, VX-702 or VX-745.

L17  ANSWER 2 OF 119  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   2005:1154543  HCAPLUS
DN   143:422248
TI   Preparation of morpholinylmethylthiophenes p38 map kinase
     modulators for the treatment of cancer
IN   Gill, Adrian Liam; Carr, Maria Grazia; Lyons, John Francis; Thompson, Neil
     Thomas; Rees, David Charles
PA   Astex Technology Limited, UK; Gill, Adrian Liam; Carr, Maria Grazia;
     Lyons, John Francis; Thompson, Neil Thomas; Rees, David Charles
SO   PCT Int. Appl., 106 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
```

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005100338	A1	20051027	WO 2005-GB1350	20050413

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI	GB 2004-8239	A	20040413
	US 2004-561600P	P	20040413
	US 2004-618830P	P	20041014

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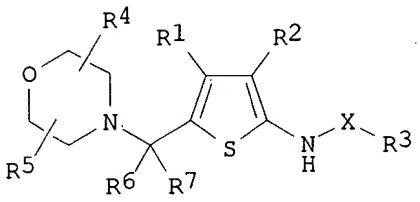

I

AB Title compds. I [R1-2 = H, alkyl, halo, CN; X = CO, CS, CONH, etc.; R3 = (hetero)aryl; R4-5 = H, Me or one of R4 and R5 is selected from CH2OH and Et and the other is H; R6-7 = H, Me] are prepared For instance, N-[4-Chloro-3-methyl-5-((morpholin-4-yl)methyl)thiophen-2-yl]-3-fluoro-5-(morpholin-4-yl)benzamide is prepared in 10 steps from 3,5-difluorobenzoic acid, morpholine and 3-chloro-4-methylthiophene-2-carboxylic acid Me ester. All example compds. exhibit IC50 < 5 μM for **p38** kinase. I are useful for the treatment of cancer.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:1075811 HCAPLUS
DN 143:367523
TI Preparation of monosaccharide derivatives as anti-inflammatory agents
IN Sattigeri, Viswajanani Jitendra; Arora, Sudershan K.; Salman, Mohammad; Palle, Venkata P.; Yadav, Gyan Chand; Tanwar, Madan Pal; Mukherjee, Ashis; Narayanan, Ramamurthy; Rauf, Abdul Rehaman Abdul; Naik, Keshav Prabhakar; Soni, Ajay; Ray, Abhijit; Shirumalla, Raj Kumar; Mookhtiar, Kasim Abbas
PA Ranbaxy Laboratories Limited, India
SO PCT Int. Appl., 185 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005092907	A2	20051006	WO 2005-IB803	20050329

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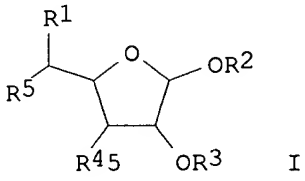
SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2004-556936P P 20040326

GI



I

AB Monosaccharide derivs. I, wherein R1 is H, alkyl, alkenyl, heterocycle, heteroaryl,alkynyl, aryl, alkoxy, acyl; R2 and R3 together form a five-membered acetal; R4 is H, OR, R is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocycle, heteroarylalkyl, heterocyclylakyl, OR; R5 is OC(O)-substituted-amine, alkyl, alkylamine, heteroaryl, heterocycle; R1R5 together form heterocycle, were prepared as anti-inflammatory agents. The compds. disorder herein can be useful for inhibition and prevention of inflammation and associated pathologies including inflammatory and autoimmune diseases such as bronchial **asthma**, **rheumatoid** arthritis, type I diabetes, multiple sclerosis, allograft rejection or psoriasis. Pharmacol. compns. containing compds. disclosed herein and the methods of treating bronchial **asthma**, chronic obstructive pulmonary disease, **rheumatoid** arthritis, multiple sclerosis, type I diabetes, psoriasis, allograft rejection, and other inflammatory and/or autoimmune disorders, using the compds. are also provided. Title monosaccharides, e.g. 1,2-O-isopropylidene-3-O-dodecyl-5-O-[[4-(2-methoxy-2-oxo-ethyl)phenyl]amino]-carbonyl-6-deoxy-α-D-glucofuranoside, were tested as inhibitors of 5-lipoxygenase with IC50 values are between about 9.5 μM and about 0.1 μM.

L17 ANSWER 4 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:490261 HCAPLUS
DN 143:19989
TI Methods and compositions for the treatment of immunoinflammatory disorders using pyrazolopyridine compounds in combination with corticosteroids or other agents
IN Jost-Price, Edward Roydon; Manivasakam, Palaniyandi; Smith, Brendan; Slavonic, Michael S.; Auspitz, Benjamin A.
PA Combinatorx, Incorporated, USA
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005051293	A2	20050609	WO 2004-US38512	20041117

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,

NE, SN, TD, TG

	US 2005187203	A1	20050825	US 2004-992878	20041119
PRAI	US 2003-524117P	P	20031121		

OS MARPAT 143:19989

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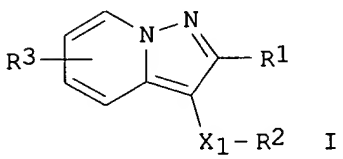

I

AB The invention features a method for treating an immunoinflammatory disorder by administering I (R1, R2 = H, C1-7 alkyl, C2-7 alkenyl C2-7 alkynyl, C2-6 heterocyclyl, etc.; R3 = H, halo, alkoxy, C1-4 alkyl; X1 = C=O, C=N-NH-R4, etc.; R4 = H, acyl), e.g., ibudilast or KC-764, alone or in combination with a corticosteroid, tetra-substituted pyrimidopyrimidine, or other compound The invention also features pharmaceutical compns. including the combination above for the treatment or prevention of an immunoinflammatory disorder. The combination of ibudilast and prednisolone reduced proinflammatory IL-1 and TNFα secretion by white blood cells stimulated by PMA-ionomycin in vitro.

L17 ANSWER 5 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:470256 HCAPLUS

DN 143:20052

TI Urea derivatives as kinase modulators

IN Milanov, Zdravko V.; Patel, Hitesh K.; Grotzfeld, Robert M.; Mehta, Shamal A.; Andiliy, Lai G.; Lockhart, David J.

PA Ambit Biosciences Corporation, USA

SO PCT Int. Appl., 350 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005048948	A2	20050602	WO 2004-US38288	20041115
	WO 2005048948	A3	20050728		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005148605	A1	20050707	US 2004-989745	20041115
US 2005165031	A1	20050728	US 2004-989814	20041115
US 2005165024	A1	20050728	US 2004-989824	20041115
US 2005165074	A1	20050728	US 2004-990007	20041115
US 2005171171	A1	20050804	US 2004-989766	20041115
US 2005171172	A1	20050804	US 2004-989823	20041115
US 2005192314	A1	20050901	US 2004-990195	20041115
US 2005197371	A1	20050908	US 2004-990194	20041115
US 2005261315	A1	20051124	US 2004-989623	20041115
US 2005267182	A1	20051201	US 2004-989717	20041115
PRAI US 2003-520273P	P	20031113		
US 2003-527094P	P	20031203		
US 2003-531082P	P	20031218		
US 2003-531243P	P	20031218		

OS MARPAT 143:20052
AB The invention provides methods and compns. for treating conditions mediated by various kinases wherein derivs. of urea compds. are employed. The invention also provides methods of using the compds. and/or compns. in the treatment of a variety of diseases and unwanted conditions in subjects such as cellular proliferative disorders.

L17 ANSWER 6 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:369225 HCAPLUS
DN 142:404248
TI Tetrasubstituted pyrimidopyrimidines, alone or in combination with other agents, for the treatment of immunoinflammatory disorders
IN Keith, Curtis; Borisy, Alexis; Zimmermann, Grant R.; Jost-Price, Edward Roydon; Manivasakam, Palaniyandi; Hurst, Nicole; Foley, Michael A.; Slavonic, Michael S.; Smith, Brendan; Auspitz, Benjamin A.
PA Combinatorx, Incorporated, USA
SO PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005037203	A2	20050428	WO 2004-US33656	20041013
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2005119160	A1	20050602	US 2004-966228	20041015
PRAI	US 2003-512415P	P	20031015		

AB The invention discloses a method for treating a patient diagnosed with, or at risk of developing, an immunoinflammatory disorder by administering to the patient a tetrasubstituted pyrimidopyrimidine, either alone or in combination with one or more addnl. agents. The invention also features a composition containing a tetra-substituted pyrimidopyrimidine in combination with one or more addnl. agents.

L17 ANSWER 7 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:177881 HCAPLUS
DN 142:274025
TI Methods using a combination of a **p38** MAP kinase inhibitor with another active agent for the treatment of chronic obstructive pulmonary disease (COPD) and pulmonary hypertension
IN Gupta, Abhya; Iacono, Philippe Didier; Kelash-Cannavo, Linda Jean; Madwed, Jeffrey B.; Park, Jung-Yong; Way, Susan Lynn; Yazdanian, Mehran
PA Boehringer Ingelheim Pharmaceuticals, Inc., USA; Boehringer Ingelheim Pharma GmbH & Co. KG; Boehringer Ingelheim France S.A.S.
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005018624	A2	20050303	WO 2004-US27013	20040819
	WO 2005018624	A3	20050506		
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TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005148555 A1 20050707 US 2004-921448 20040819
PRAI US 2003-497376P P 20030822
AB Methods are disclosed for treating COPD and pulmonary hypertension using **p38** MAP Kinase inhibitors in combination with one or more other active ingredients.

L17 ANSWER 8 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:99319 HCAPLUS
DN 142:172181
TI Novel targets of protein kinase-inhibiting drugs for novel disease therapies
IN Biggs, William H., III; Carter, Todd; Fabian, Miles A.; Lockhart, David J.; Zarrinkar, Patrick Parvis; Treiber, Daniel Kelly; Edeen, Phillip
PA Ambit Biosciences Corporation, USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005009367	A2	20050203	WO 2004-US23325	20040719
WO 2005009367	A3	20050512		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-488513P P 20030717
AB The invention is directed to the identification and use of addnl. targets of BIRB 796, imatinib mesylate, and BAY 43-9006. The new targets of BIRB 796, imatinib mesylate, and BAY 43-9006 can be used to screen for suitable therapeutic compds. Also, novel therapeutic and prophylactic uses for BIRB 796, imatinib mesylate, and BAY 43-9006 are disclosed herein. Protein targets of the drugs were identified using a phage-based competition assay using a panel of 69 proteins including 48 kinases.

L17 ANSWER 9 OF 119 USPATFULL on STN
AN 2005:234133 USPATFULL
TI Compositions, combinations, and methods for treating cardiovascular conditions and other associated conditions
IN Rudolph, Amy E., Fairfield, CT, UNITED STATES
Rocha, Ricardo, Flemington, NJ, UNITED STATES
PI US 2005203072 A1 20050915
AI US 2004-787721 A1 20040226 (10)
PRAI US 2003-450529P 20030226 (60)
DT Utility
FS APPLICATION
LREP Julie M. Lappin, Pharmacia Corporation, Mail Zone MC5S, 575 Maryville Centre Drive, St. Louis, MO, 63141, US
CLMN Number of Claims: 48
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 6548
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention is directed generally to a method for treating a

pathological condition (particularly a cardiovascular condition (e.g., hypertension or heart failure) or a condition associated with a cardiovascular condition) using a **p38**-kinase inhibitor (e.g., a **p38**-kinase-inhibiting substituted pyrazole), and specifically a combination comprising a **p38**-kinase inhibitor with an aldosterone antagonist or diuretic for treating a cardiovascular condition. This invention also is directed generally to combinations comprising a **p38**-kinase inhibitor, and specifically to combinations comprising a **p38**-kinase inhibitor with an aldosterone antagonist or diuretic. This invention is further directed generally to pharmaceutical compositions comprising a **p38** -kinase inhibitor, and more specifically to compositions comprising the above-described combinations.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 10 OF 119 USPATFULL on STN
AN 2005:215527 USPATFULL
TI Methods and reagents for the treatment of inflammatory disorders
IN Jost-Price, Edward Roydon, West Roxbury, MA, UNITED STATES
Manivasakam, Palaniyandi, Brighton, MA, UNITED STATES
Smith, Brendan, Boston, MA, UNITED STATES
Slavonic, Michael S., Quincy, MA, UNITED STATES
Auspitz, Benjamin A., Cambridge, MA, UNITED STATES
PI US 2005187203 A1 20050825
AI US 2004-992878 A1 20041119 (10)
PRAI US 2003-524117P 20031121 (60)
DT Utility
FS APPLICATION
LREP CLARK & ELBING LLP, 101 FEDERAL STREET, BOSTON, MA, 02110, US
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2781
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention features a method for treating an immunoinflammatory administering a compound of formula (I), e.g., ibudilast or KC-764, alone or in combination with a corticosteroid, tetra-substituted pyrimidopyrimidine, or other compound. The invention also features pharmaceutical compositions including the combination above for the treatment or prevention of an immunoinflammatory disorder.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 11 OF 119 USPATFULL on STN
AN 2005:208498 USPATFULL
TI Extracellular TNF inhibitors for treating CNS disorders
IN Shafer, Lisa L., Stillwater, MN, UNITED STATES
PA Medtronic, Inc., Minneapolis, MN, UNITED STATES (U.S. corporation)
PI US 2005180974 A1 20050818
AI US 2004-972177 A1 20041022 (10)
PRAI US 2003-514137P 20031024 (60)
DT Utility
FS APPLICATION
LREP MEDTRONIC, INC., 710 MEDTRONIC PARKWAY NE, MS-LC340, MINNEAPOLIS, MN, 55432-5604, US
CLMN Number of Claims: 55
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 790
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods and devices to attenuate tumor necrosis factor (TNF) and other pro-inflammatory mediators in the CNS to treat neurological, neurodegenerative, neuropsychiatric disorders, and brain injury are described. More particularly, TNF blocking agents that target TNF-receptor interactions and the effects of downstream secreted cytokines associated with an inflammatory cascade are described. Such TNF blocking agents are administered directly to the brain by, for

example, intraparenchymal administration, intracerebroventricular administration, or administration into a cerebral artery. Devices described include therapy delivery devices comprising a reservoir capable of housing a TNF blocking agent and a catheter operably coupled to the device and adapted to deliver the TNF blocking agent to a target site within a subject.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 12 OF 119 USPATFULL on STN
AN 2005:184022 USPATFULL
TI Anticoagulant and fibrinolytic therapy using **p38** MAP kinase inhibitors
IN Wood, Chester C., Ridgefield, CT, UNITED STATES
van der Poll, Tom, Amsterdam, NETHERLANDS
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, UNITED STATES (U.S. corporation)
Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, GERMANY, FEDERAL REPUBLIC OF (U.S. corporation)
PI US 2005159417 A1 20050721
AI US 2004-9480 A1 20041210 (11)
RLI Continuation of Ser. No. US 2003-630599, filed on 30 Jul 2003, ABANDONED
PRAI US 2002-403422P 20020814 (60)
DT Utility
FS APPLICATION
LREP MICHAEL P. MORRIS, BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877-0368, US
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3491
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are methods for a treating a disease or condition relating to blood coagulation and fibrinolysis using **p38** MAP kinase inhibitors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 13 OF 119 USPATFULL on STN
AN 2005:177291 USPATFULL
TI Conjugated small molecules
IN Grotzfeld, Robert M., Carlsbad, CA, UNITED STATES
Milanov, Zdravko V., San Diego, CA, UNITED STATES
Patel, Hitesh K., Encinitas, CA, UNITED STATES
Lai, Andiliy G., San Diego, CA, UNITED STATES
Mehta, Shamal A., San Diego, CA, UNITED STATES
Lockhart, David J., Del Mar, CA, UNITED STATES
PA Ambit Biosciences Corporation (U.S. corporation)
PI US 2005153371 A1 20050714
AI US 2005-31638 A1 20050107 (11)
PRAI US 2004-535173P 20040107 (60)
US 2004-557941P 20040330 (60)
DT Utility
FS APPLICATION
LREP WILSON SONSINI GOODRICH & ROSATI, 650 PAGE MILL ROAD, PALO ALTO, CA, 943041050, US
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 1662
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Provided herein are linker compounds and conjugates that include the linker compounds. In one embodiment, the linker compounds comprise 2 or 3 residues of 6-aminohexanoic acid and optionally 7-10 residues of polyethyleneglycol (PEG). The linker compounds are useful in forming conjugates with one or more components useful in biopharmaceutical or bioanalytical applications. In particular, the biopharmaceutically useful compounds are kinase inhibitors. The conjugates described herein

have utility in a variety of diagnostic, separation, and therapeutic applications.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 14 OF 119 USPATFULL on STN
AN 2005:171806 USPATFULL
TI Methods of treating COPD and pulmonary hypertension
IN Gupta, Abhya, Biberach an der Riss, GERMANY, FEDERAL REPUBLIC OF
Iacono, Philippe Didier, Betheny, FRANCE
Kelash-Cannavo, Linda Jean, Newtown, CT, UNITED STATES
Madwed, Jeffrey B., Trumbull, CT, UNITED STATES
Park, Jung-Yong, Danbury, CT, UNITED STATES
Way, Susan Lynn, Danbury, CT, UNITED STATES
Yazdanian, Mehran, Philadelphia, PA, UNITED STATES
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, UNITED STATES (non-U.S. corporation)
Boehringer Ingelheim International GmbH, Ingelheim, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)
Boehringer Ingelheim France, Reims Cedex, FRANCE (non-U.S. corporation)
PI US 2005148555 A1 20050707
AI US 2004-921448 A1 20040819 (10)
PRAI US 2003-497376P 20030822 (60)
DT Utility
FS APPLICATION
LREP MICHAEL P. MORRIS, BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877-0368, US
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1252
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are methods of treating COPD and Pulmonary Hypertension using **p38** Map Kinase inhibitors in combination with one or more other active ingredients.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 15 OF 119 USPATFULL on STN
AN 2005:158985 USPATFULL
TI Polymorphs
IN Smoliga, John A., Brookfield, CT, UNITED STATES
Vitous, Jana, Danbury, CT, UNITED STATES
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, UNITED STATES (U.S. corporation)
PI US 2005137195 A1 20050623
AI US 2004-10975 A1 20041213 (11)
PRAI US 2003-530834P 20031218 (60)
DT Utility
FS APPLICATION
LREP MICHAEL P. MORRIS, BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877-0368, US
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 268
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are polymorphs of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea and processes from making the same.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 16 OF 119 USPATFULL on STN
AN 2005:144880 USPATFULL
TI Pharmaceutical compounds
IN Frederickson, Martyn, Cambridge, UNITED KINGDOM
Gill, Adrian Liam, Cambridge, UNITED KINGDOM

Padova, Alessandro, Roma, ITALY
Congreve, Miles Stuart, Cambridge, UNITED KINGDOM
PI US 2005124620 A1 20050609
AI US 2004-962085 A1 20041008 (10)
RLI Continuation of Ser. No. WO 2003-GB1507, filed on 8 Apr 2003, UNKNOWN
PRAI GB 2002-8248 20020409
GB 2002-15180 20020629
DT Utility
FS APPLICATION
LREP HESLIN ROTHENBERG FARLEY & MESITI PC, 5 COLUMBIA CIRCLE, ALBANY, NY, 12203, US
CLMN Number of Claims: 23
ECL Exemplary Claim: 1-67
DRWN No Drawings
LN.CNT 2017
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds are disclosed of the formula (I): ##STR1## in which U, T, V and W are each a nitrogen atom or carbon atom. When U, T, V or W is a carbon atom, it may be substituted. The compounds are inhibitors of **p38** MAP kinase and are useful for treating inflammatory diseases such as arthritis. An example of such a compound is: ##STR2##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 17 OF 119 USPATFULL on STN
AN 2005:111168 USPATFULL
TI Techniques to treat neurological disorders by attenuating the production of pro-inflammatory mediators
IN Shafer, Lisa L., Stillwater, MN, UNITED STATES
PA Medtronic, Inc., Minneapolis, MN, UNITED STATES (U.S. corporation)
PI US 2005095246 A1 20050505
AI US 2004-972157 A1 20041022 (10)
PRAI US 2003-514137P 20031024 (60)
DT Utility
FS APPLICATION
LREP MEDTRONIC, INC., 710 MEDTRONIC PARKWAY NE, MS-LC340, MINNEAPOLIS, MN, 55432-5604, US
CLMN Number of Claims: 89
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 1408
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods and devices to attenuate tumor necrosis factor (TNF) and other pro-inflammatory mediators in the CNS to treat neurological, neurodegenerative, neuropsychiatric disorders, pain and brain injury are described. More particularly, TNF blocking agents that target intracellular signals and downstream effects associated with the production and secretion of TNF are described. Devices described include therapy delivery devices comprising a reservoir capable of housing a TNF blocking agent and a catheter operably coupled to the device and adapted to deliver the TNF blocking agent to a target site within a subject.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 18 OF 119 USPATFULL on STN
AN 2005:44298 USPATFULL
TI Novel bicyclic urea derivatives useful in the treatment of cancer and other disorders
IN Dumas, Jacques, Bethany, CT, UNITED STATES
Boyer, Stephen, Fairfield, CT, UNITED STATES
Verma, Sharad, New Haven, CT, UNITED STATES
Adnane, Lila, Madison, CT, UNITED STATES
Chen, Yuanwei, North Haven, CT, UNITED STATES
Lee, Wendy, Hamden, CT, UNITED STATES
Phillips, Barton, New Haven, CT, UNITED STATES
Smith, Roger A., Madison, CT, UNITED STATES
Scott, William J., Guildford, CT, UNITED STATES
Burke, Jennifer, New Haven, CT, UNITED STATES

Chen, Jianqing, New Haven, CT, UNITED STATES
Chen, Zhi, Hamden, CT, UNITED STATES
Fan, Jianmei, Hamden, CT, UNITED STATES
Miranda, Karl, North Haven, CT, UNITED STATES
Raudenbush, Brian, Charlton, MA, UNITED STATES
Redman, Aniko, Derby, CT, UNITED STATES
Shao, Jianxing, Acton, MA, UNITED STATES
Su, Ning, Hamden, CT, UNITED STATES
Wang, Gan, Wallingford, CT, UNITED STATES
Yi, Lin, Milford, CT, UNITED STATES
Zhu, Qingming, West Haven, CT, UNITED STATES

PI US 2005038031 A1 20050217
AI US 2004-788426 A1 20040301 (10)
PRAI US 2003-450323P 20030228 (60)
US 2003-450324P 20030228 (60)
DT Utility
FS APPLICATION
LREP MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4157
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to novel diaryl ureas, pharmaceutical compositions containing such compounds and the use of those compounds or compositions for treating hyper-proliferative and angiogenesis disorders, as a sole agent or in combination with cytotoxic therapies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 19 OF 119 USPATFULL on STN
AN 2005:38118 USPATFULL
TI 2-Oxo-1,3,5-perhydrotriazapine derivatives useful in the treatment of hyper-proliferative, angiogenesis, and inflammatory disorders
IN Boyer, Stephen, Fairfield, CT, UNITED STATES
Dumas, Jacques, Bethany, CT, UNITED STATES
Phillips, Barton, New Haven, CT, UNITED STATES
Scott, William J., Guildford, CT, UNITED STATES
Smith, Roger A., Madison, CT, UNITED STATES
Chen, Jianqing, New Haven, CT, UNITED STATES
Jones, Benjamin, Hamden, CT, UNITED STATES
Wang, Gan, Wallingford, CT, UNITED STATES

PI US 2005032798 A1 20050210
AI US 2004-788405 A1 20040301 (10)
PRAI US 2003-450323P 20030228 (60)
US 2003-450324P 20030228 (60)
US 2003-450348P 20030228 (60)
DT Utility
FS APPLICATION
LREP MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2600
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to novel diaryl ureas, pharmaceutical compositions containing such compounds and the use of those compounds or compositions for treating hyper-proliferative and angiogenesis disorders, as a sole agent or in combination with cytotoxic therapies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 20 OF 119 USPATFULL on STN
AN 2005:10965 USPATFULL
TI Assays and kits for detecting protein binding
IN Lockhart, David J., Del Mar, CA, UNITED STATES

Zarrinkar, Patrick Parvis, San Diego, CA, UNITED STATES
Treiber, Daniel Kelly, San Diego, CA, UNITED STATES
PA Ambit Biosciences Corporation, San Diego, CA (U.S. corporation)
PI US 2005009099 A1 20050113
AI US 2004-873835 A1 20040621 (10)
PRAI US 2003-480587P 20030620 (60)
DT Utility
FS APPLICATION
LREP WILSON SONSINI GOODRICH & ROSATI, 650 PAGE MILL ROAD, PALO ALTO, CA, 943041050
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)
LN.CNT 1539
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides methods for determining the interactions between phage-displayed proteins and test molecules. The phage-displayed proteins are contacted with a reference moiety in the presence and absence of a test molecule; the behavior of the phage-displayed proteins as a function of concentration of the test molecule permits calculation of the binding affinity of the phage-displayed protein for the test molecule.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 21 OF 119 USPATFULL on STN
AN 2005:270550 USPATFULL
TI Biarylurea derivatives
IN Hayama, Takashi, Tsukuba, JAPAN
Hayashi, Kyoko, Tsukuba, JAPAN
Honma, Teruki, Tsukuba, JAPAN
Takahashi, Ikuko, Tsukuba, JAPAN
PA Banyu Pharmaceutical Co., Ltd., Tokyo, JAPAN (non-U.S. corporation)
PI US 6958333 B1 20051025
WO 2001007411 20010201
AI US 2001-31795 20000726 (10)
WO 2000-JP4991 20000726
20020402 PCT 371 date
PRAI JP 2001-211384 19990726
DT Utility
FS GRANTED
EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Habte, Kahsay
LREP Wenderoth, Lind & Ponack, L.L.P.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 11452
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a compound of Formula (I) and the manufacturing method(s) thereof and the use thereof: ##STR1## wherein: Ar is a nitrogen-containing heteroaromatic ring group; X and Z are each a carbon atom, and so on; Y is CO, and so on; R.sub.1 is a hydrogen atom, and so on; R.sub.2 and R.sub.3 are each a hydrogen atom, and so on; R.sub.4 and R.sub.5 are each a hydrogen atom, and so on; and the formula ##CUSTOM-CHARACTER-00001## is a single bond or a double bond. According to the present invention, the compound of the present invention can provide Cdk4 and/or Cdk6 inhibitors for treating malignant tumors, because the compounds of the present invention exhibit a prominent growth inhibitory activity against tumor cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 22 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:418520 HCAPLUS
DN 143:111403
TI BIRB796 Inhibits All **p38** MAPK Isoforms in Vitro and in Vivo
AU Kuma, Yvonne; Sabio, Guadalupe; Bain, Jenny; Shpiro, Natalia; Marquez, Rodolfo; Cuenda, Ana

CS Medical Research Council Protein Phosphorylation Unit, University of Dundee, Dundee, DD1 5EH, UK
SO Journal of Biological Chemistry (2005), 280(20), 19472-19479
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB The compound BIRB796 inhibits the stress-activated protein kinases **p38**.alpha. and **p38**.beta. and is undergoing clin. trials for the treatment of inflammatory diseases. Here we report that BIRB796 also inhibits the activity and the activation of SAPK3/**p38** γ. This occurs at higher concns. of BIRB796 than those that inhibit **p38**.alpha. and **p38**.beta. and at lower concns. than those that inhibit the activation of JNK isoforms. We also show that at these concns., BIRB796 blocks the stress-induced phosphorylation of the scaffold protein SAP97, further establishing that this is a physiol. substrate of SAPK3/**p38**.gamma.. Our results demonstrate that BIRB796, in combination with SB203580, a compound that inhibits **p38**.alpha. and **p38**.beta., but not the other **p38** isoforms, can be used to identify physiol. substrates of SAPK3/**p38**.gamma. as well as those of **p38**.alpha. and **p38**.beta..
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 23 OF 119 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 2
AN 2005:453017 BIOSIS
DN PREV200510241416
TI Inhibition of drug-resistant mutants of ABL, KIT, and EGF receptor kinases.
AU Carter, Todd A.; Wodicka, Lisa M.; Shah, Neil P.; Velasco, Anne Marie; Fabian, Miles A.; Treiber, Daniel K.; Milanov, Zdravko V.; Atteridge, Corey E.; Biggs, William H. III; Edeen, Philip T.; Floyd, Mark; Ford, Julia M.; Grotzfeld, Robert M.; Herrgard, Sanna; Insko, Darren E.; Mehta, Shamal A.; Patel, Hitesh K.; Pao, William; Sawyers, Charles L.; Varmus, Harold; Zarrinkar, Patrick P. [Reprint Author]; Lockhart, David J.
CS Ambit Inc, 4215 Sorrento Valley Blvd, San Diego, CA 92121 USA
pzarrinkar@ambitbio.com; dlockhart@ambitbio.com
SO Proceedings of the National Academy of Sciences of the United States of America, (AUG 2 2005) Vol. 102, No. 31, pp. 11011-11016.
CODEN: PNASA6. ISSN: 0027-8424.
DT Article
LA English
ED Entered STN: 3 Nov 2005
Last Updated on STN: 3 Nov 2005
AB To realize the full potential I of targeted protein kinase inhibitors for the treatment of cancer, it is important to address the emergence of drug resistance in treated patients. Mutant forms of BCR-ABL, KIT, and the EGF receptor (EGFR) have been found that confer resistance to the drugs imatinib, gefitinib, and erlotinib. The mutations weaken or prevent drug binding, and interestingly, one of the most common sites of mutation in all three kinases is a highly conserved "gatekeeper" threonine residue near the kinase active site. We have identified existing clinical compounds that bind and inhibit drug-resistant mutant variants of ABL, KIT, and EGFR. We found that the Aurora kinase inhibitor VX-680 and the **p38** inhibitor BIRB-796 inhibit the imatinib- and BMS-354825-resistant ABL(T315I) kinase. The KIT/FLT3 inhibitor SU-111248 potently inhibits the imatinib-resistant KIT(V559D/T670I) kinase, consistent with the clinical efficacy of SU-11248 against imatinib-resistant gastrointestinal tumors, and the EGFR inhibitors EKB-569 and CI-1033, but not GW-572016 and ZD-6474, potently inhibit the gefitinib- and erlotinib-resistant EGFR(L858R/T790M) kinase. EKB-569 and CI-1033 are already in clinical trials, and our results suggest that they should be considered for testing in the treatment of gefitinib/erlotinib-resistant non-small cell lung cancer. The results highlight the strategy of screening existing clinical compounds against newly identified drug-resistant mutant variants to find compounds that may serve as starting points for the development of next-generation drugs, or that

could be used directly to treat patients that have acquired resistance to first-generation targeted therapy.

L17 ANSWER 24 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:301463 HCAPLUS
DN 143:3640
TI HierS: Hierarchical Scaffold Clustering Using Topological Chemical Graphs
AU Wilkens, Steven J.; Janes, Jeff; Su, Andrew I.
CS Genomics Institute of the Novartis Research Foundation, San Diego, CA, 92121, USA
SO Journal of Medicinal Chemistry (2005), 48(9), 3182-3193
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB An exhaustive ring-based algorithm, HierS, has been developed in order to provide an intuitive approach to compound clustering for analyzing high-throughput screening results. The recursive algorithm rapidly identifies all possible ring-delimited substructures within a set of compds. Mols. are grouped by shared ring substructures (scaffolds) so that common scaffolds obtain higher membership. Once all of the scaffolds for a set of compds. are identified, the hierarchical structural relationships between the scaffold structures are established. The complex network of hierarchical relationships is then utilized to navigate compds. in a structurally directed fashion. When the scaffold hierarchy is traversed, over-represented structural features can be rapidly identified so that excess compds. that contain them can be removed without significantly impacting the structural diversity landscape of the compound set. Furthermore, the removed compds. can provide the opportunity to follow-up on active compds. that had previously been discarded because of practical limitations on follow-up capacity. A Web-based interface has been developed that incorporates this algorithm in order to allow for an interactive anal. In addition, biol. data are coupled to scaffolds by the inclusion of activity histograms, which indicate how the compds. in each scaffold class performed in previous high-throughput screening campaigns.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 25 OF 119 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 2005504606 EMBASE
TI Pathway to the clinic: Inhibition of **P38** MAP kinase. A review of ten chemotypes selected for development.
AU Goldstein D.M.; Gabriel T.
CS D.M. Goldstein, Department of Medicinal Chemistry, Roche Palo Alto, 3431 Hillview Ave., Palo Alto, CA 94304, United States. david-m.goldstein@roche.com
SO Current Topics in Medicinal Chemistry, (2005) Vol. 5, No. 10, pp. 1017-1029.
Refs: 44
ISSN: 1568-0266 CODEN: CTMCCL
CY Netherlands
DT Journal; General Review
FS 026 Immunology, Serology and Transplantation
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
ED Entered STN: 20051128
Last Updated on STN: 20051128
AB **p38** mitogen activated protein (MAP) kinase remains the most compelling therapeutic target for oral drug intervention for a wide range of autoimmune disorders based on the central role this enzyme plays in inflammatory cell signaling, Efforts to discover inhibitors of **p38** suitable for clinical investigation have continued to escalate in part due to the incredible diversity of unique chemotypes reported to inhibit the

enzyme. Since 1993, at least seventeen **p38** inhibitors have been reported to have entered into clinical trials. Next generation inhibitors have been disclosed with improved potency for **p38** and enhanced selectivity versus other protein kinases. Over the last three years, there have been multiple reports of cytokine suppression in humans following oral administration of **p38** inhibitors. These results, in addition to proof of concept studies in **rheumatoid** patients, have established **p38** inhibition as an avenue for the future management of pro-inflammatory cytokine based diseases. This review describes the discovery at Roche of novel **p38** inhibitors which have advanced into clinical trials. The pharmacology of the Roche compounds is then compared with eight chemically distinct **p38** inhibitors known to have entered clinical development. .COPYRGT. 2005 Bentham Science Publishers Ltd.

L17 ANSWER 26 OF 119 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 2005504605 EMBASE
TI Structural comparison of **p38** inhibitor-protein complexes: A review of recent **p38** inhibitors having unique binding interactions.
AU Wrobleski S.T.; Doweyko A.M.
CS S.T. Wrobleski, Department of Discovery Chemistry, Bristol-Myers Squibb, P.O. Box 4000, Princeton, NJ 08543-4000, United States. stephen.wrobleski@bms.com
SO Current Topics in Medicinal Chemistry, (2005) Vol. 5, No. 10, pp. 1005-1016.
Refs: 80
ISSN: 1568-0266 CODEN: CTMCCL
CY Netherlands
DT Journal; General Review
FS 030 Pharmacology
037 Drug Literature Index
LA English
SL English
ED Entered STN: 20051128
Last Updated on STN: 20051128
AB Small molecule inhibition of protein kinases in the treatment of significant diseases such as cancer, Alzheimer's disease, diabetes, and **rheumatoid** arthritis has attracted significant attention over the past two decades and has clearly become one of the most significant challenges for drug discovery in the 21st century. While the recent identification of 518 different kinases in the human genome has offered a wealth of opportunities for drug intervention in the treatment of these diseases, it has also created a daunting challenge with respect to selective kinase inhibition as a viable strategy in target-based drug design. Over the past decade, the design and development of a small molecule that selectively inhibits the **p38** mitogen activated protein (MAP) kinase has clearly emerged as one of these challenges within the industry. This review will focus on the comparison of the x-ray crystal structures and binding models of the most recent **p38** inhibitor-enzyme complexes and the identification of the structural elements and interactions that may be important in providing inhibitor potency and selectivity toward the **p38** MAP kinase. .COPYRGT. 2005 Bentham Science Publishers Ltd.

L17 ANSWER 27 OF 119 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 2005473373 EMBASE
TI Second-generation kinase inhibitors.
AU Klebl B.M.; Muller G.
CS Dr. B.M. Klebl, GPC Biotech AG, Max-Lebsche-Platz 32, D-81377 Munich, Germany. Bert.Klebl@gpc-biotech.com
SO Expert Opinion on Therapeutic Targets, (2005) Vol. 9, No. 5, pp. 975-993.
Refs: 91
ISSN: 1472-8222 CODEN: EOTTAO
CY United Kingdom
DT Journal; General Review

FS 016 Cancer
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
ED Entered STN: 20051110
Last Updated on STN: 20051110
AB An increasing number of kinase inhibitor candidates are entering clinical development, representing an important change in the pharmaceutical industry; notably, the development of small-molecule kinase inhibitors for signal transduction therapies. Today, kinase inhibitors garner substantial attention in cancer research. Over the last few years, three distinct small-molecule kinase inhibitors reached the market for treatment of chronic myeloid leukaemia, gastrointestinal stromal tumours, and non-small cell lung cancers. These three drugs, imatinib, gefitinib and erlotinib, act on a distinct subset of dysregulated, and often cancer-relevant kinases. Imatinib, gefitinib and erlotinib are considered the front-runners of targeted kinase inhibitor drugs. The entire research field gains tremendous insights through the ongoing research and clinical trials with these three drugs and with fast following first-generation kinase inhibitors, many of which are in different phases of clinical development. In addition, novel chemogenomic and chemoproteomic technologies are emanating from the current kinase research area, focussing efforts on the generation of spectrum-selective inhibitors for anticancer therapies as opposed to the monospecific inhibitors for the remaining therapeutic areas.

L17 ANSWER 28 OF 119 EMBASE
AN 2005504603 EMBASE
TI Small molecule **p38** inhibitors: Novel structural features and advances from 2002-2005.
AU Hynes Jr. J.; Leftheris K.
CS J. Hynes Jr., Department of Discovery Chemistry, Pharmaceutical Research Institute, Bristol-Myers Squibb, PO Box 4000, Princeton, NJ 08543-4000, United States. john.hynes@bms.com
SO Current Topics in Medicinal Chemistry, (2005) Vol. 5, No. 10, pp. 967-985.
Refs: 153
ISSN: 1568-0266 CODEN: CTMCCL
CY Netherlands
DT Journal; General Review
FS 026 Immunology, Serology and Transplantation
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
ED Entered STN: 20051128
Last Updated on STN: 20051128
AB The discovery and development of selective, efficacious, and safe small molecule **p38** mitogen-activated protein kinase inhibitors for the treatment of inflammatory diseases remains the focus of many pharmaceutical research programs. Advances in small molecule **p38** inhibitor design in potency and oral efficacy have been accelerated with the large number of available inhibitor-enzyme x-ray structures. These advances have allowed for the discovery of diverse sets of inhibitors with the opportunity to map inhibitor interactions and design selective inhibitors. This review covers recent compound disclosures in the patent and published literature over the last three years. Many disclosures represent new chemotypes as well as creative modifications of known structures.

L17 ANSWER 29 OF 119 EMBASE
AN 2005504602 EMBASE
TI The discovery of novel chemotypes of **p38** kinase inhibitors.
AU Diller D.J.; Lin T.H.; Metzger A.

CS D.J. Diller, Department of Molecular Modeling, Pharmacopeia Inc., CN5350, Princeton, NJ 08543-5350, United States. ddiller@pharmacop.com
SO Current Topics in Medicinal Chemistry, (2005) Vol. 5, No. 10, pp. 953-965. Refs: 85
ISSN: 1568-0266 CODEN: CTMCCL
CY Netherlands
DT Journal; General Review
FS 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
ED Entered STN: 20051128
Last Updated on STN: 20051128
AB In the late 1970s and the early 1980s the initial **p38** chemotype, the triaryl imidazoles, was discovered as an off-target effect during the development of cyclooxygenase and 5-lipoxygenase inhibitors long before the identity of the **p38** kinase was known. During the last 10 years a number of novel **p38** chemotypes were discovered via high throughput screening. More recently, the first series of **p38** inhibitors discovered by xray crystallographic and virtual screening was announced. Finally, throughout the life span of **p38** drug discovery programs significant medicinal chemistry effort has continually been placed on the design of new inhibitors from known chemotypes using molecular modeling, protein crystallography, hybrid design and simply sound intuition. Indeed, the search for **p38** kinase inhibitors offers an excellent historical perspective as to how technological changes that have taken place in the pharmaceutical industry over the last decade, have affected the ways in which new leads are discovered and advanced. It is the intent of this review to highlight the discoveries of novel **p38** chemotypes, emphasizing where possible the key technologies used in the discoveries and the knowledge gained from each discovery. .COPYRGT. 2005 Bentham Science Publishers Ltd.

L17 ANSWER 30 OF 119 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 2005504601 EMBASE
TI Discovery of highly selective inhibitors of **p38**.alpha..
AU Popa-Burke I.; Birkos S.; Blackwell L.; Cheatham L.; Clark J.; Dickson Jr. J.K.; Galasinski S.; Janzen W.P.; Mendoza J.; Miller J.L.; Mohney R.P.; Steed P.M.; Hodge C.N.
CS I. Popa-Burke, Amphora Discovery Corporation, P.O. Box 12169, Research Triangle Park, NJ 27709, United States. Ioana.Popa-Burke@amphoracorp.com
SO Current Topics in Medicinal Chemistry, (2005) Vol. 5, No. 10, pp. 941-951. Refs: 35
ISSN: 1568-0266 CODEN: CTMCCL
CY Netherlands
DT Journal; General Review
FS 030 Pharmacology
037 Drug Literature Index
LA English
SL English
ED Entered STN: 20051128
Last Updated on STN: 20051128
AB The **p38** MAP kinases are a family of serine/threonine protein kinases that play a key role in cellular pathways leading tp pro-inflammatory responses. We have developed and implemented a method for rapidly identifying and optimizing potent and selective **p38** α inhibitors, which is amenable to other targets and target classes. A diverse library of druggable, purified and quantitated molecules was assembled and standardized enzymatic assays were performed in a microfluidic format that provided very accurate and precise inhibition data allowing for development of SAR directly from the primary HTS. All compounds were screened against a collection of more than 60 enzymes (kinases, proteases and phosphatases), allowing for removal of promiscuous and non-selective inhibitors very early in the discovery process. Follow-up enzymological studies included measurement of concentration of compound in buffer, yielding accurate determination of K(i) and IC(50)

values, as well as mechanism of action. In addition, active compounds were screened against less desirable properties such as inhibition of the enzyme activity by aggregation, irreversible binding, and time-dependence. Screening of an 88,634-compound library through the above-described process led to the rapid identification of multiple scaffolds (>5 active compounds per scaffold) of potential drug leads for **p38**.alpha. that are highly selective against all other enzymes tested, including the three other **p38** isoforms. Potency and selectivity data allowed prioritization of the identified scaffolds for optimization. Herein we present results around our 3-thio-1,2,4-triazole lead series of **p38**.alpha. selective inhibitors, including identification, SAR, synthesis, selectivity profile, enzymatic and cellular data in their progression towards drug candidates. .COPYRGT. 2005 Bentham Science Publishers Ltd.

L17 ANSWER 31 OF 119 EMBASE
AN 2005504600 EMBASE
TI Potential adverse effects associated with inhibition of **p38** α/β MAP kinases.
AU Dambach D.M.
CS D.M. Dambach, Department of Discovery Toxicology, Bristol Myers Squibb, Pharmaceuticals Research Institute, Princeton, NJ 08543, United States. Donna.Dambach@bms.com
SO Current Topics in Medicinal Chemistry, (2005) Vol. 5, No. 10, pp. 929-939. Refs: 145
ISSN: 1568-0266 CODEN: CTMCCL
CY Netherlands
DT Journal; General Review
FS 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
052 Toxicology
LA English
SL English
ED Entered STN: 20051128
Last Updated on STN: 20051128
AB Inhibitors of **p38** MAP kinases show promise for the treatment of inflammatory and immunological disorders and some cancers. There is a substantial body of experimental evidence across several organ systems suggesting that **p38** also mediates developmental, differentiation and proliferation processes. As a consequence of the wide-ranging regulatory role of **p38** kinase in diverse cellular processes, the possibility of adverse events resulting from undesired pharmacological activity is a major concern for the **p38** inhibitor drug class. Taking into consideration the limitations of experimental modeling systems, together the data may indicate that profound inhibition of **p38** has the potential to impact these processes during fetal or neonatal development. The difficulty comes in extrapolating these findings to predict potential adverse effects under conditions of partial inhibition of **p38** activity, and in an adult population in which these processes are typically only recapitulated during repair or adaptive responses. As such, the goal of this review of the targets of **p38** activity is to bring an awareness of the those organ systems that should be monitored for potential toxicity, as well as to present a potential mechanistic basis for such monitoring or for investigation of adverse effects that may develop with administration of a **p38** inhibitor. .COPYRGT. 2005 Bentham Science Publishers Ltd.

L17 ANSWER 32 OF 119 EMBASE
AN 2005504599 EMBASE
TI The biology of **p38** kinase: A central role in inflammation.
AU Schieven G.L.
CS G.L. Schieven, Bristol-Myers Squibb Pharmaceutical Research Institute, P.O. Box 4000, Princeton, NJ 08543, United States. gary.schieven@bms.com
SO Current Topics in Medicinal Chemistry, (2005) Vol. 5, No. 10, pp. 921-928.

Refs: 64
ISSN: 1568-0266 CODEN: CTMCCL
CY Netherlands
DT Journal; General Review
FS 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
ED Entered STN: 20051128
Last Updated on STN: 20051128
AB The **p38** kinase plays a central role in inflammation, and it has been the subject of extensive efforts in both basic research and drug discovery. This review summarizes the biology of the **p38** kinase with a focus on its role in inflammation. The **p38** kinase regulates the production of key inflammatory mediators, including TNFα, IL-1β, and COX-2. In addition, **p38** also acts downstream of cytokines such as TNFα, mediating some of their effects. The potential efficacy of **p38** inhibitors may thus be greater than would be expected from the inhibition of the mediators alone. Inhibitors of **p38** kinase are currently in development for the treatment of **rheumatoid** arthritis. The biological processes regulated by **p38** kinase suggest a wide variety of additional potential indications. .COPYRGT. 2005 Bentham Science Publishers Ltd.

L17 ANSWER 33 OF 119 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 2005376746 EMBASE
TI Structure-activity relationships of **p38** Mitogen-Activated protein kinase inhibitors.
AU Bolos J.
CS J. Bolos, Prous Institute for Collaborative Biomedical Research, 08028 Barcelona, Spain. JORDI-BOLOS@terra.es
SO Mini-Reviews in Medicinal Chemistry, (2005) Vol. 5, No. 9, pp. 857-868.
Refs: 117
ISSN: 1389-5575 CODEN: MMCIAE
CY Netherlands
DT Journal; General Review
FS 029 Clinical Biochemistry
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
052 Toxicology
LA English
SL English
ED Entered STN: 20050915
Last Updated on STN: 20050915
AB **Rheumatoid** arthritis and other chronic inflammatory diseases constitute a major therapeutic challenge, usually not sufficiently met by the classical antiinflammatory medications. Recent research efforts provided new insights into the molecular basis of these pathologies and disclosed new opportunities for developing improved drugs directed to the chemical mediators of the disease. The enzyme **p38** MAP kinase plays a central role in the signal transduction cascade that leads to the production of both the proinflammatory cytokines, TNF-α and IL-1β, thus representing an attractive therapeutic target for novel antiinflammatory therapies. A number of **p38** inhibitors belonging to different structural families have been developed as potential antiinflammatory drugs, and some of them progressed into clinical trials. The initial pyridinyl imidazole inhibitors contributed to the identification and characterization of **p38** MAP kinase as the molecular target of these new drugs, and were found to act as competitive inhibitors at the ATP binding site of the enzyme. A number of variations in the pyridine and imidazole rings were subsequently introduced. Other inhibitors structurally unrelated to the

pyridinylimidazoles have also been developed, such as the pyridopyridazinones, diaryl ureas, aminobenzophenones and aromatic amides. One of these structural classes, the N,N'-diarylureas, has been found to interact with a distinct allosteric site of **p38** MAP kinase and requires a deep conformational change prior to binding. .COPYRGT. 2005 Bentham Science Publishers Ltd.

L17 ANSWER 34 OF 119 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 2005333012 EMBASE
TI **p38** inhibitors: Beyond pyridinylimidazoles.
AU Dominguez C.; Tamayo N.; Zhang D.
CS C. Dominguez, Amgen Inc., One Amgen Center Drive, Thousands Oaks, CA 91320, United States. celiad@amgen.com
SO Expert Opinion on Therapeutic Patents, (2005) Vol. 15, No. 7, pp. 801-816. Refs: 41
ISSN: 1354-3776 CODEN: EOTPEG
CY United Kingdom
DT Journal; General Review
FS 029 Clinical Biochemistry
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LA English
SL English
ED Entered STN: 20050825
Last Updated on STN: 20050825
AB Since the discovery of **p38** mitogen-activated protein kinase (MAPK) as a potential intracellular modulator that regulates the crucial biosynthesis and functions of pro-inflammatory cytokines (e.g., TNF-α and IL-1β), numerous groups have disclosed their efforts to find small-molecule **p38** inhibitors as potential therapeutic agents for the treatment of inflammatory diseases such as **rheumatoid** arthritis (RA), **Crohn**'s disease (CD) and psoriasis. Although greater selectivity has been achieved with these newly disclosed series, their safety profile after chronic treatment remains a question to be answered in human clinical trials. The **p38** inhibitors that have been disclosed in the recent patent literature (2000 - 2004) are summarised here. These compounds will be classified into series based on their intrinsic structures and by their binding modes, as revealed by either crystallography or molecular modelling. .COPYRGT. 2005 Ashley Publications Ltd.

L17 ANSWER 35 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:250810 HCAPLUS
DN 143:71273
TI The discovery of novel protein kinase inhibitors by using fragment-based high-throughput X-ray crystallography
AU Gill, Adrian; Cleasby, Anne; Jhoti, Harren
CS Astex Technology, Cambridge, CB4 0QA, UK
SO ChemBioChem (2005), 6(3), 506-512
CODEN: CBCHFX; ISSN: 1439-4227
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
AB This article describes the application of a high-throughput x-ray crystallog. fragment-based screening methodol. to identify low-mol.-weight leads for structure-based optimization into protein kinase inhibitors. The identification of 2 novel **p38**.alpha. MAP kinase inhibitors (with IC50=65 and 150 nM) starting from low-mol.-weight fragments is described.
RE.CNT 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 36 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:594355 HCAPLUS

TI **p38** MAP kinase inhibitors: Many are made, but few are chosen
AU Dominguez, Celia; Powers, David A.; Tamayo, Nuria
CS Chemistry Research & Discovery Medicinal Chemistry, Amgen Inc, Thousand Oaks, CA, 91320-179, USA
SO Current Opinion in Drug Discovery & Development (2005), 8(4), 421-430
CODEN: CODDFF; ISSN: 1367-6733
PB Thomson Scientific
DT Journal; General Review
LA English
AB A review. T he mitogen-activated protein kinase (MAPK) **p38** is a Ser/Thr kinase, originally isolated from lipopolysaccharide-stimulated monocytes. There are 4 isoforms of the enzyme (**p38**.alpha., **p38**.beta., **p38**.gamma. and **p38**.delta.), which differ in tissue distribution, regulation of kinase activation, and subsequent phosphorylation of downstream substrates. These enzymes also differ in sensitivity to **p38** MAPK inhibitors. The most thoroughly studied isoform is **p38**.alpha., for which activation was observed in many hematopoietic and non-hematopoietic cell types upon appropriate stimuli. **p38**.alpha. kinase is involved in the biosynthesis of the cytokines tumor necrosis factor-α and interleukin-1β at the translational and transcriptional level. MAPK **p38**.alpha. represents a point of convergence for multiple signaling processes that are activated during inflammation, making it a key potential target for the modulation of cytokine production The discovery and publication of **p38**.alpha. and a pyridinyl-imidazole-based **p38**.alpha. inhibitor initiated a huge effort by many companies to develop **p38**.alpha. inhibitors as potential treatments for inflammatory diseases. Herein, a brief overview is provided of the discovery and development of AMG-548 (Amgen Inc), a selective and efficacious **p38**.alpha. inhibitor, and its pharmacodynamic effects in a 1st-in-human study. Data from a phase I multidose clin. trial are also included. In addition, other **p38**.alpha. inhibitors that have advanced to clin. trials over the last 3 years are discussed, such as BIRB-796 (Boehringer Ingelheim Pharmaceuticals Inc). SCIO-469 and SCIO-323 (Scios Inc), and VX-702 (Vertex Pharmaceuticals Inc/Kissei Pharmaceutical Co).
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 37 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:1141975 HCAPLUS
DN 142:190235
TI Identification of Novel **p38**.alpha. MAP Kinase Inhibitors Using Fragment-Based Lead Generation
AU Gill, Adrian L.; Frederickson, Martyn; Cleasby, Anne; Woodhead, Steven J.; Carr, Maria G.; Woodhead, Andrew J.; Walker, Margaret T.; Congreve, Miles S.; Devine, Lindsay A.; Tisi, Dominic; O'Reilly, Marc; Seavers, Lisa C. A.; Davis, Deborah J.; Curry, Jayne; Anthony, Rachel; Padova, Alessandro; Murray, Christopher W.; Carr, Robin A. E.; Jhoti, Harren
CS Astex Technology, Cambridge, CB4 0QA, UK
SO Journal of Medicinal Chemistry (2005), 48(2), 414-426
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 142:190235
AB We describe the structure-guided optimization of the mol. fragments 2-amino-3-benzyloxypyridine 1 (IC50 1.3 mM) and 3-(2-(4-pyridyl)ethyl)indole 2 (IC50 35 μM) identified using X-ray crystallog. screening of **p38**.alpha. MAP kinase. Using two sep. case studies, the article focuses on the key compds. synthesized, the structure-activity relationships and the binding mode observations made during this optimization process, resulting in two potent lead series that demonstrate significant increases in activity. We describe the process of compound elaboration either through the growing out from fragments into adjacent pockets or through the conjoining of overlapping fragments and demonstrate that we have exploited the mobile conserved activation loop, consisting in part of Asp168-Phe169-Gly170 (DFG), to generate significant

improvements in potency and kinase selectivity.
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 38 OF 119 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 3
AN 2005:196873 BIOSIS
DN PREV200500191049
TI A small molecule-kinase interaction map for clinical kinase inhibitors.
AU Fabian, Miles A.; Biggs, William H. III; Treiber, Daniel K.; Atteridge, Corey E.; Azimioara, Mihai D.; Benedetti, Michael G.; Carter, Todd A.; Ciceri, Pietro; Edeen, Philip T.; Floyd, Mark; Ford, Julia M.; Galvin, Margaret; Gerlach, Jay L.; Grotzfeld, Robert M.; Herrgard, Sanna; Insko, Darren E.; Insko, Michael A.; Lai, Andiliy G.; Lelias, Jean-Michel; Mehta, Shamal A.; Milanov, Zdravko V.; Velasco, Anne Marie; Wodicka, Lisa M.; Patel, Hitesh K.; Zarrinkar, Patrick P.; Lockhart, David J. [Reprint Author]
CS Ambit Biosci, 4215 Sorrento Valley Blvd, San Diego, CA, 92121, USA pzarrinkar@ambitbio.com; dlockhart@ambitbio.com
SO Nature Biotechnology, (March 2005) Vol. 23, No. 3, pp. 329-336. print. ISSN: 1087-0156 (ISSN print).
DT Article
LA English
ED Entered STN: 25 May 2005
Last Updated on STN: 25 May 2005
AB Kinase inhibitors show great promise as a new class of therapeutics. Here we describe an efficient way to determine kinase inhibitor specificity by measuring binding of small molecules to the ATP site of kinases. We have profiled 20 kinase inhibitors, including 16 that are approved drugs or in clinical development, against a panel of 119 protein kinases. We find that specificity varies widely and is not strongly correlated with chemical structure or the identity of the intended target. Many novel interactions were identified, including tight binding of the **p38** inhibitor BIRB-796 to an imatinib-resistant variant of the ABL kinase, and binding of imatinib to the SRC-family kinase LICK. We also show that mutations in the epidermal growth factor receptor (EGFR) found in gefitinib-responsive patients do not affect the binding affinity of gefitinib or erlotinib. Our results represent a systematic small molecule-protein interaction map for clinical compounds across a large number of related proteins.

L17 ANSWER 39 OF 119 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 2005247144 EMBASE
TI Doramapimod.
AU Mealy N.E.; Bayes M.
CS N.E. Mealy, Prous Science, P.O. Box 540, 08080 Barcelona, Spain
SO Drugs of the Future, (2005) Vol. 30, No. 2, pp. 198. ISSN: 0377-8282 CODEN: DRFUD4
CY Spain
DT Journal; Note
FS 031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
ED Entered STN: 20050630
Last Updated on STN: 20050630
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L17 ANSWER 40 OF 119 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 2005247112 EMBASE
TI Annual update 2004/2005 - Treatment of musculoskeletal disorders.
AU Prous J.R.
SO Drugs of the Future, (2005) Vol. 30, No. 2, pp. 181-186. ISSN: 0377-8282 CODEN: DRFUD4
CY Spain
DT Journal; General Review
FS 031 Arthritis and Rheumatism

037 Drug Literature Index
LA English
ED Entered STN: 20050630
Last Updated on STN: 20050630
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L17 ANSWER 41 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:1072170 HCAPLUS
DN 142:190226
TI Interaction Profiles of Protein Kinase-Inhibitor Complexes and Their Application to Virtual Screening
AU Chuaqui, Claudio; Deng, Zhan; Singh, Juswinder
CS Computational Drug Design Group, Department of Research Informatics, Biogen Idec, Inc., Cambridge, MA, 01242, USA
SO Journal of Medicinal Chemistry (2005), 48(1), 121-133
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB A major challenge facing structure-based drug discovery efforts is how to leverage the massive amount of exptl. (x-ray and NMR) and virtual structural information generated from drug discovery projects. Many important drug targets have large nos. of protein-inhibitor complexes, necessitating tools to compare and contrast their similarities and differences. This information would be valuable for understanding potency and selectivity of inhibitors and could be used to define target constraints to assist virtual screening. The authors describe a profile-based approach that enables us to capture the conservation of interactions between a set of protein-ligand receptor complexes. The use of profiles provides a sensitive means to compare multiple inhibitors binding to a drug target. The authors demonstrate the utility of profile-based anal. of small mol. complexes from the protein-kinase family to identify similarities and differences in binding of ATP, **p38**, and CDK2 compds. to kinases and how these profiles can be applied to differentiate the selectivity of these inhibitors. Importantly, our virtual screening results demonstrate superior enrichment of kinase inhibitors using profile-based methods relative to traditional scoring functions. Interaction-based anal. should provide a valuable tool for understanding inhibitor binding to other important drug targets.
RE.CNT 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 42 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:610501 HCAPLUS
DN 143:243882
TI Time-resolved Forster resonance energy transfer assays for the binding of nucleotide and protein substrates to protein kinase
AU Zhang, Wen Xiao; Wang, Ruixiu; Wisniewski, Douglas; Marcy, Alice I.; LoGrasso, Philip; Lisnock, Jean-Marie; Cummings, Richard T.; Thompson, James E.
CS Merck Research Laboratories, Rahway, NJ, 07065, USA
SO Analytical Biochemistry (2005), 343(1), 76-83
CODEN: ANBCA2; ISSN: 0003-2697
PB Elsevier
DT Journal
LA English
AB The authors have developed assays for the binding of nucleotide and protein substrates to **p38**.alpha. protein kinase based on time-resolved Forster resonance energy transfer. **P38**.alpha. was biotinylated by addition of a sequence that targets biotin to a single lysine when coexpressed with biotin ligase in Escherichia coli, allowing formation of a complex between a streptavidin "LANCE" europium chelate conjugate and **p38**.alpha.. When this reagent was combined with M39AF, a **p38** inhibitor containing a fluorescent moiety whose excitation wavelengths match the emission wavelengths of the europium chelate, a change in ratio of light emitted at 665 nm/615 nm is detected. Less than 100 pM complex was detected with a signal/background ratio of >30-fold. The complex exhibits slow, tight binding kinetics where the

apparent Kd decreases with a relaxation time of 21 min at 125 pM biotin-**p38**.alpha.. Preincubating inhibitors or ATP with biotin-**p38**.alpha. and adding M39AF as a competitor yielded IC50s consistent with those measured by enzyme assay for the activated form of biotin-**p38**.alpha.. The same technique was also used to measure affinity of inhibitors for the unphosphorylated and catalytically inactive form of biotin-**p38**.alpha.. To measure affinity of **p38** α for its protein substrate MK2, the authors incubated biotin-**p38**.alpha. with a glutathione S-transferase MK2 fusion protein. Detection of the complex after incubation with streptavidin-allophycocyanin and a LANCE-conjugated anti-GST allowed measurement of affinity of MK2 for biotin-**p38**.alpha. and detection of 0.5 nM **p38**.alpha. · MK2 complex with signal/background ratio >5-fold. Competition with unbiotinylated **p38**.alpha. yielded an IC50 value of 5 nM. Activation of either **p38**.alpha. or MK2 had no effect on the measured Kd. M39AF was found to bind in a ternary complex with **p38**.alpha.·MK2 with lower affinity than that observed in the binary complex with **p38**.alpha. alone.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 43 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4
AN 2004:995770 HCAPLUS
DN 141:406057
TI Methods and reagents for the treatment of diseases and disorders associated with increased levels of proinflammatory cytokines
IN Jost-Price, Edward Roydon; Manivasakam, Palaniyandi; Smith, Brendan; Fong, Jason; Auspitz, Benjamin A.; Nichols, M. James; Keith, Curtis; Zimmermann, Grant R.; Brasher, Bradley B.; Sachs, Noah; Chappell, Todd W.
PA USA
SO U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U.S. Ser. No. 670,488.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004229849	A1	20041118	US 2004-777517	20040212
	US 2004220153	A1	20041104	US 2003-670488	20030924
	US 2005153947	A1	20050714	US 2004-947455	20040920
	WO 2005030132	A2	20050407	WO 2004-US31195	20040923
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2005112199	A1	20050526	US 2004-947769	20040923
	WO 2005079284	A2	20050901	WO 2005-US4297	20050211
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2002-413040P	P	20020924		
	US 2002-417261P	P	20021009		
	US 2002-427424P	P	20021119		

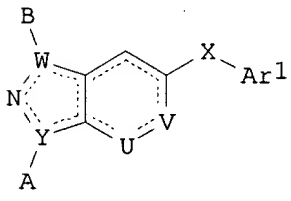
US 2002-427526P	P	20021119
US 2003-464753P	P	20030423
US 2003-670488	A2	20030924
US 2003-512415P	P	20031015
US 2003-520446P	P	20031113
US 2004-777517	A1	20040212
US 2004-777518	A	20040212
US 2004-557496P	P	20040330
US 2004-944574	A	20040920
US 2004-947455	A	20040922

AB The invention features a method for treating a patient diagnosed with, or at risk of developing, an immunoinflammatory disorder by administering an SSRI or analog or metabolite thereof and, optionally, a corticosteroid or other compound to the patient. The invention also features a pharmaceutical composition containing an SSRI or analog or metabolite thereof and a corticosteroid or other compound for the treatment or prevention of an immunoinflammatory disorder.

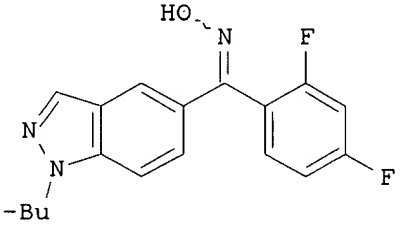
L17 ANSWER 44 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5
AN 2004:802552 HCAPLUS
DN 141:314320
TI Preparation of indazoles and related compounds as **p38** inhibitors
IN Munson, Mark; Mareska, David A.; Kim, Youngboo; Groneberg, Robert D.; Rizzi, James; Rodriguez, Martha; Kim, Ganghyeok; Vigers, Guy; Rao, Chang; Balachari, Devan; Harvey, Darren
PA USA
SO U.S. Pat. Appl. Publ., 139 pp., Cont.-in-part of U.S. Ser. No. 688,849.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004192653	A1	20040930	US 2004-788044	20040225
US 2004176325	A1	20040909	US 2003-378164	20030303
US 2004180896	A1	20040916	US 2003-688849	20031015
PRAI US 2003-378164	A2	20030303		
US 2003-688849	A2	20031015		

OS MARPAT 141:314320
GI



I



II

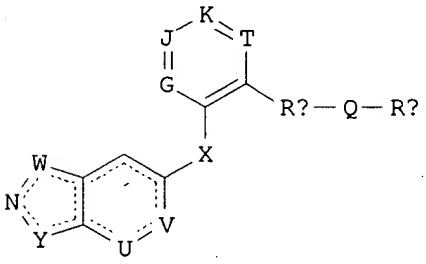
AB The invention provides for the preparation of the title compds. I [Y = C, N; W = C, N, S, provided that W = N, S, or O when Y = C, and W = C or N when Y = N; U = CH, N; V = C(E), N; X = O, S, SO, SO2, etc.; Ar1 = (un)substituted (hetero)aryl; A = H, OH, an amine protecting group, etc.; B = H, NH2, (un)substituted Me; E = H, OH, an amine protecting group, etc.; with the provisos; and stereoisomers, solvates, and pharmaceutically acceptable salts thereof] as **p38** MAP kinase inhibitors. For example, cyclization of 4-bromo-2-methylaniline with NH4BF4 provided 5-bromo-1H-indazole, which was N-alkylated with 1-bromo-2-methylpropane (50.8% over 2 steps). Coupling with 2,4-difluorobenzaldehyde (69.1%), followed by oxidation (75.6%) and reaction with NH2OH•HCl (65.5%) gave (2,4-difluorophenyl)(1-isobutyl-1H-indazol-5-yl)methanone oxime (II). The

latter inhibited **p38**.alpha. activity and LPS-induced TNF-α secretion from human peripheral blood mononuclear cells (PBMC) with IC50 values <500 nM. The invention also provides pharmaceutical compns. comprising I and methods of using the inhibitors and pharmaceutical compns. in the treatment and prevention of various disorders mediated by **p38**, such as inflammatory disease, autoimmune disease, destructive bone disorder, proliferative disorder, infectious disease, viral disease, or neurodegenerative disease (no data).

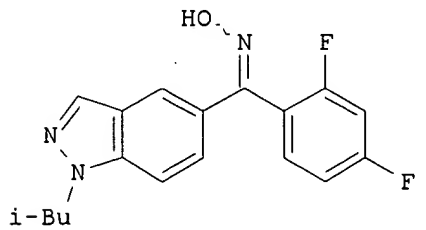
L17 ANSWER 45 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6
AN 2004:759826 HCAPLUS
DN 141:260746
TI Preparation of indazoles and related compounds as **p38** inhibitors
IN Munson, Mark; Kim, Youngboo; Groneberg, Robert D.; Rizzi, James; Rodriguez, Martha; Kim, Ganghyeok; Vigers, Guy; Rao, Chang; Balachari, Devan
PA USA
SO U.S. Pat. Appl. Publ., 118 pp., Cont.-in-part of U.S. Pat. Appl. 2004 176,325.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004180896	A1	20040916	US 2003-688849	20031015
	US 2004176325	A1	20040909	US 2003-378164	20030303
	CA 2517517	AA	20040916	CA 2004-2517517	20040225
	WO 2004078116	A2	20040916	WO 2004-US5693	20040225
	WO 2004078116	A3	20041014		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004192653	A1	20040930	US 2004-788044	20040225
PRAI	US 2003-378164	A2	20030303		
	US 2003-688849	A	20031015		
	WO 2004-US5693	W	20040225		

OS MARPAT 141:260746
GI



I



II

AB The invention provides for the preparation of title compds. I [wherein G, J, K, T = independently NCRz; Q = NR8CONH, NHCO, NR8SO2NH, NHSO2, COR11; U, V = (un)substituted CH, N; W = CR3, N, NR4; X = O, S, SO, SO2, NR5, CO, CH2, CH2ZnOH, C=NORd; Y = CR1, O, S, NR2; Z = (un)substituted alk(en/yn)ylene; R1, R2 = independently H, OH, amine-protecting group, ZnNRaRb, ZnNRaCORb, ZnSO2Ra, ZnSORa, ZnSRa, ZnORa, ZnCORa, ZnCO2Ra, ZnOCORa, (un)substituted (hetero)alk(en/yn)yl, (hetero)alkoxy, Zn-(hetero)cycloalkyl, ZnAr1; R3 = H, NH2, F, Cl, (un)substituted Me; R4, R5 = independently H, (un)substituted Me; R6 = H, CF3, (hetero)alkyl; R8, R11 = independently H, alkyl; Ra, Rb = independently H, OH, amine-, alc.-, or sulfur-protecting group, (un)substituted (hetero)alk(en/yn)yl, (hetero)alkoxy, Zn-(hetero)cycloalkyl, ZnAr1; or NRaRb = (un)substituted heterocyclyl; Rd = H, PO3H2, SO3H, (un)substituted (hetero)alk(en/yn)yl, (hetero)alkoxy, Zn-(hetero)cycloalkyl, ZnAr1; Rx = (un)substituted (CH2)m, O(CH2)m, NH(CH2)m, S(CH2)m; Ry = H, PO3H2, amine- or oxygen-protecting group, (un)substituted (hetero)alk(en/yn)yl, (hetero)alkoxy, Zn-(hetero)cycloalkyl, ZnAr1; Rz = H, F, Cl, Br, CF3, OR6, SR6, alkyl, CN, (un)substituted NH2; Ar1 = (un)substituted (hetero)aryl; m = 1-3; with provisos; and stereoisomers, solvates, and pharmaceutically acceptable salts thereof] as **p38** MAP kinase inhibitors. For example, cyclization of 4-bromo-2-methylaniline with NH4BF4 provided 5-bromo-1H-indazole, which was N-alkylated with 1-bromo-2-methylpropane (50.8% over 2 steps). Coupling with 2,4-difluorobenzaldehyde (69.1%), followed by oxidation (75.6%) and reaction with NH2OH•HCl (43.1%) gave (2,4-difluorophenyl)(1-isobutyl-1H-indazol-5-yl)methanone oxime (II). The latter inhibited **p38**.alpha. activity and LPS-induced TNF-α secretion from human peripheral blood mononuclear cells (PBMC) with IC50 values <500 nM. The invention also provides pharmaceutical compns. comprising I and methods of using the inhibitors and pharmaceutical compns. in the treatment and prevention of various disorders mediated by **p38**, such as inflammatory disease, autoimmune disease, destructive bone disorder, proliferative disorder, infectious disease, viral disease, or neurodegenerative disease (no data).

L17 ANSWER 46 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 7
AN 2004:701815 HCAPLUS
DN 141:185104
TI Compositions, combinations, and methods for treating cardiovascular conditions and other associated conditions
IN Rudolph, Amy E.; Rocha, Ricardo; Carretero, Oscar
PA USA
SO U.S. Pat. Appl. Publ., 107 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004167197	A1	20040826	US 2004-788220	20040226
	WO 2004075852	A2	20040910	WO 2004-US5609	20040226
	WO 2004075852	A3	20050728		

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	WO 2004075857	A2	20040910	WO 2004-US5799	20040226
	WO 2004075857	A3	20050818		

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,

ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005203072 A1 20050915 US 2004-787721 20040226
PRAI US 2003-450529P P 20030226

AB This invention is directed generally to a method for treating a pathol. condition (particularly a cardiovascular condition (e.g., hypertension or heart failure) or a condition associated with a cardiovascular condition) using a **p38**-kinase inhibitor (e.g., a **p38**-kinase-inhibiting substituted pyrazole), and specifically a combination comprising a **p38**-kinase inhibitor with an angiotensin-converting-enzyme inhibitor (or "ACE inhibitor") for treating a cardiovascular condition. This invention also is directed generally to combinations comprising a **p38**-kinase inhibitor, and specifically to combinations comprising a **p38**-kinase inhibitor with an angiotensin-converting-enzyme inhibitor. This invention is further directed generally to pharmaceutical compns. comprising a **p38**-kinase inhibitor, and more specifically to compns. comprising the above-described combinations.

L17 ANSWER 47 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 8
AN 2004:142601 HCAPLUS
DN 140:193063
TI Anticoagulant and fibrinolytic therapy using **p38** MAP kinase inhibitors
IN Wood, Chester C.; Van Der Poll, Tom
PA Boehringer Ingelheim Pharmaceuticals, Inc., Germany; Boehringer Ingelheim Pharma GmbH & Co. KG
SO U.S. Pat. Appl. Publ., 47 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004033222	A1	20040219	US 2003-630599	20030730
	CA 2496445	AA	20040226	CA 2003-2496445	20030730
	WO 2004016267	A1	20040226	WO 2003-US23841	20030730

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	EP 1545514	A1	20050629	EP 2003-788293	20030730

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

	US 2005159417	A1	20050721	US 2004-9480	20041210
PRAI	US 2002-403422P	P	20020814		
	US 2003-630599	B1	20030730		
	WO 2003-US23841	W	20030730		

AB Disclosed are methods for a treating a disease or condition relating to blood coagulation and fibrinolysis using **p38** MAP kinase inhibitors. 1-(3-Tert-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-[4-(2-morpholin-4-ylethoxy)naphthalen-1-yl]urea, preparation given, was tested in humans.

L17 ANSWER 48 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:1156620 HCAPLUS

DN 142:71185
TI Phage display assay for detecting protein binding by screening libraries of compounds against phage-displayed polypeptides
IN Lockhart, David J.; Zarrinkar, Patrick Parvis; Treiver, Daniel Kelly
PA Ambit Biosciences, Inc., USA; Ambit Biosciences Corporation
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004113556	A2	20041229	WO 2004-US19943	20040621
	WO 2004113556	C1	20050310		
	WO 2004113556	A3	20051103		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2005009099	A1	20050113	US 2004-873835	20040621
PRAI	US 2003-480587P	P	20030620		

AB The present invention provides methods and kits for identifying interactions between test mols. and polypeptides. Preferably the polypeptides are displayed on phage and the interactions are evaluated in the presence of reference moieties that are optionally attached to a solid support. One aspect of the invention is a method for determining the binding affinities of a test mol. to different polypeptides from a set of polypeptides. In another aspect, the invention provides a method of screening libraries of compds. against one or more polypeptides. The present invention also provides methods of quantifying the interaction between phage-displayed polypeptides and test mols. Kits for performing the assays described herein are also provided. The invention is based on the ability to assess the affinity of the interaction, if any, of a test mol. and a phage-displayed polypeptide in the presence of a reference moiety that binds the displayed polypeptide. The test mol. may be considered as a competitor against the reference moiety for binding to the displayed polypeptide. Therefore, in one aspect, the invention is directed to a method to apply phage display technol., wherein the method comprises simultaneously contacting a phage-displayed polypeptide with a reference moiety immobilized on a solid support and a test mol. at a sufficient concentration to decrease the binding of the displayed polypeptide to the reference moiety. The concns. of the test mol. necessary to diminish binding of the displayed polypeptide from the reference moiety may be used to determine a dissociation constant (Kd) for the test mol. Human kinases expressed as fusions to T7 bacteriophage particles and a small set of immobilized ligands that bind to the ATP site of one or more kinases were used. Six compds. were tested for the ability to compete with the interaction between **p38** and immobilized SB202190: SB202190 (without biotin modification); SB203580 (a pyridinylimidazole closely related to SB202190) (Table 1); SB202474 (a pyridinylimidazole that does not bindp 38); BIRB-796 (Table 1); VX-745 (Table 1); and purvalanol A (a CDK2 inhibitor). Competition with unmodified SB202190, SB203580, BIRB-796 and VX-745 decreased by 1000-fold or more the amount of phage-displayed **p38** bound to the solid support, whereas neither SB202474 nor purvalanol A had a significant effect (Fig. 1B). These results demonstrate that the binding assay correctly discriminates between compds. that bind to the kinase, and those that do not, and yields accurate binding consts.

L17 ANSWER 49 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:1016023 HCAPLUS
DN 142:6557

TI Preparation of nitrogenous heterocyclic compounds as **p38** MAP kinase inhibitors
IN Takahashi, Kanji; Sumino, Naoki; Yamamoto, Shingo; Sugitani, Masafumi; Uegaki, Akihiko; Nakatani, Shingo; Matsunaga, Naoki; Inukai, Takayuki
PA Ono Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004101529	A1	20041125	WO 2004-JP7070	20040518

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI JP 2003-141042	A	20030519	
JP 2003-338389	A	20030929	
JP 2004-110572	A	20040402	

OS MARPAT 142:6557
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

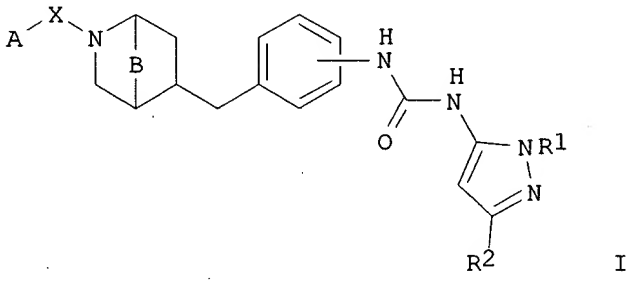
AB Title compds. I [A = H, (un)substituted cycle, etc.; B = (un)substituted cycle; E = spacer; K = C, N; Z = O, etc.; C:T = carbonyl, etc.; D = (un)substituted heterocycle containing at least one nitrogen] were prepared For example, EDCI-mediated acylation of compound II·2HCl [X = H] with 4-(N-methylpiperazinyl)methylbenzoic acid afforded compound II [X = 4-(N-methylpiperazinyl)methylbenzoyl]. In **p38** MAP (mitogen activated protein) kinase inhibition assays, the IC50 value of compound II [X = 4-(N-methylpiperazinyl)methylbenzoyl] was 2.5 nM. Compound I are claimed useful for the treatment of inflammation, cancer, etc. Formulations are given.
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 50 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:1015876 HCAPLUS
DN 142:23273
TI Preparation of pyrazolyl phenyl urea derivatives as inhibitors of **p38** kinase and/or tumor necrosis factor (TNF) inhibitors for the treatment of inflammations
IN Borcherding, David R.; Gross, Alexandre; Shum, Patrick Wai-Kwok; Willard, Nicole; Freed, Brian S.
PA Aventis Pharmaceuticals Inc., USA
SO PCT Int. Appl., 235 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004100946	A1	20041125	WO 2004-US13875	20040505

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG
PRAI US 2003-468285P P 20030506
OS MARPAT 142:23273
GI



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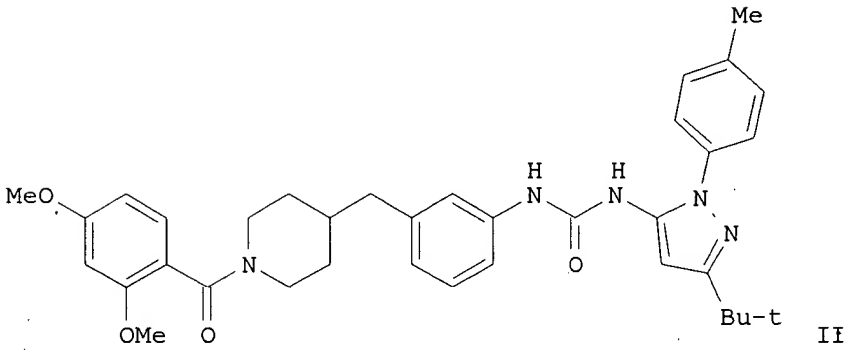


II

AB Title compds. I [Wherein R1 = (cyclo)alkyl, (un)substituted aryl or pyridyl; R2 = (un)substituted (cyclo)alkyl; X = C(O), C(O)CH2, S(O)2, or NHC(O); A = (un)substituted alk(en/yn)yl; B = (CH2)n; n = 0 or 2; et al., or pharmaceutically acceptable salts, solvates or ester prodrugs thereof; or ester prodrugs of such salts or solvates], useful as inhibitors of **p38** kinase and/or tumor necrosis factor (TNF), were prepared Thus, condensation of 4-methylenepiperidine hydrochloride with 2,4-dimethoxybenzoyl chloride followed by addition reaction with 9-BBN and subsequent Pd-catalyzed coupling with m-bromoaniline gave an aniline derivative This compound underwent addition reaction with 5-isocyanato-3-tert-butyl-1-(4-methylphenyl)pyrazole to afford urea II. Compds. I were tested in several biol. assays. E.g., I showed 50% inhibition at the concns. of 0.3-10000 nM in the **p38** cascade assay, at the concns. of 10-50000 nM in the murine **p38** assay, and at the concns. of 10-50000 nM in the LPS-induced TNFα assay. Pharmaceutical compns. comprising I are useful in the treatment of disease states capable of being modulated by the inhibition of **p38** kinase and/or tumor necrosis factor (TNF), such as **asthma** and joint inflammation.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

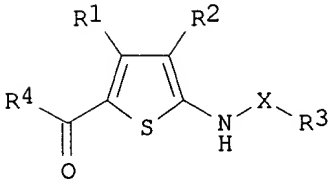
L17 ANSWER 51 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:878388 HCAPLUS
DN 141:366122
TI Preparation of 5-amino-2-carbonylthiophenes for use as **p38** MAP kinase inhibitors in the treatment of inflammatory diseases

IN Gill, Adrian Liam; Woodhead, Steven; Carr, Maria
PA Astex Technology Limited, UK
SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004089929	A1	20041021	WO 2004-GB1589	20040413

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2003-8511 A 20030414
OS MARPAT 141:366122
GI



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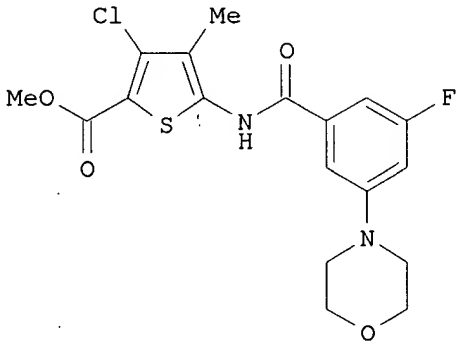


II

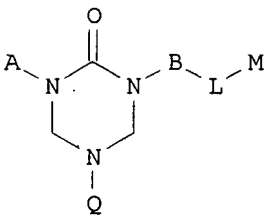
AB Title compds. I [wherein R1, R2 = independently H, alkyl, halo, CN; X = CO, CS, CONH, CSNH, CO2, COS, CSO, CS2; R3 = (un)substituted (hetero)aryl; R4 = YR5, R6; Y = NH, O, S; R5 = (un)substituted cycloalkyl, heterocyclyl, alkyl; R6 = (un)substituted heterocyclyl; or salts, solvates, or N-oxides thereof] were prepared as **p38** MAP kinase inhibitors. For example, amidation of 3-morpholino-5-fluorobenzoic acid with 3-chloro-4-methyl-5-aminothiophene-2-carboxylic acid Me ester using oxalyl chloride, DMF, and DIEA in CH2Cl2 provided II. The latter inhibited phosphorylation by **p38** MAP kinase with IC50 <15 μM. Thus, I and their pharmaceutical compns. are useful in the treatment of conditions mediated by **p38** MAP kinase, such as inflammatory and arthritic diseases (no data).
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 52 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:756709 HCAPLUS
DN 141:260780
TI Preparation of 2-oxo-1,3,5-perhydrotriazapine derivatives for treatment of hyper-proliferative, angiogenesis, and inflammatory disorders
IN Boyer, Stephen; Dumas, Jacques; Phillips, Barton; Scott, William J.; Smith, Roger A.; Chen, Jianqing; James, Benjamin; Wang, Gan
PA Bayer Pharmaceuticals Corporation, USA
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004078746	A2	20040916	WO 2004-US6283	20040301
	WO 2004078746	A3	20041202		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2516624	AA	20040916	CA 2004-2516624	20040301
	EP 1599466	A2	20051130	EP 2004-716136	20040301
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
PRAI	US 2003-450323P	P	20030228		
	WO 2004-US6283	W	20040301		

OS MARPAT 141:260780
GI



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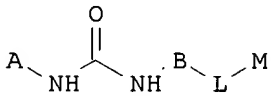
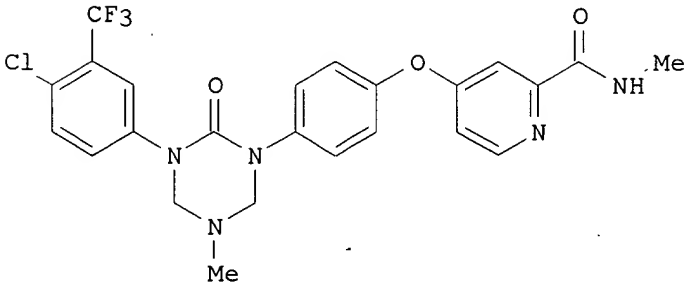


III



II

AB The title compds. I [A, B = 5-10 membered cyclic moieties which optionally substituted with 1-4 substituents selected from the group consisting of R1, OR1, NR1R2, etc.; L = a bridging group selected from -(CH2)m-O-(CH2)n-, -(CH2)m-(CH2)n-, -(CH2)m-C(O)-(CH2)n-, etc.; m, n = 0-4; M = Ph, naphthyl, 5- or 6- membered monocyclic heteroaryl consisting 1-3 heteroatoms selected from O, N, S, etc.; R1, R2 = H, alkyl, Ph, etc.] were prepared for treating hyper-proliferative and angiogenesis disorders. For example, reaction of 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-2-Pyridinecarboxamide with methylamine hydrochloride and formaldehyde furnished compound II. As prodrugs, compds. I will release diaryl ureas of the formula III when administrated.

L17 ANSWER 53 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:718295 HCAPLUS
DN 141:236648
TI Combination therapy for the treatment of immunoinflammatory disorders
IN Jost-Price, Edward Roydon; Brasher, Bradley B.; Chappel, Todd W.; Manivasakam, Palaniyandi; Sachs, Noah; Smith, Brendan; Auspitz, Benjamin

A.
PA Combinatorx, Incorporated, USA
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004073614	A2	20040902	WO 2004-US4077	20040212
	WO 2004073614	A3	20041111		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2514061	AA	20040902	CA 2004-2514061	20040212
	EP 1599212	A2	20051130	EP 2004-710606	20040212
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2005192261	A1	20050901	US 2004-940902	20040914
	WO 2005027839	A2	20050331	WO 2004-US30210	20040915
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI	US 2003-447366P	P	20030214
	US 2003-447412P	P	20030214
	US 2003-447415P	P	20030214
	US 2003-447553P	P	20030214
	US 2003-447648P	P	20030214
	US 2003-464753P	P	20030423
	US 2003-503026P	P	20030915
	WO 2004-US4077	W	20040212

AB The invention features a method for treating a patient diagnosed with, or at risk of developing, an immunoinflammatory disorder by administering a non-steroidal immunophilin-dependent immunosuppressant (NsIDI) and an NsIDI enhancer (NsIDIE) or analog or metabolite thereof to the patient. The invention also features a pharmaceutical composition containing an NsIDI and NsIDIE or analog or metabolite thereof for the treatment or prevention of an immunoinflammatory disorder.

L17 ANSWER 54 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:589376 HCAPLUS
DN 141:140433
TI Preparation of 1-pyrazolyl-3-phenylurea **p38** MAP kinase inhibitors as antiinflammatory medicaments
IN Flynn, Daniel L.; Petrillo, Peter A.
PA Deciphera Pharmaceuticals, Inc., USA; Deciphera Pharmaceuticals, LLC
SO PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004060306	A2	20040722	WO 2003-US41449	20031226
	WO 2004060306	A3	20050728		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004180906	A1	20040916	US 2003-746460	20031224
CA 2513627	AA	20040722	CA 2003-2513627	20031226
EP 1585734	A2	20051019	EP 2003-808576	20031226

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRAI US 2002-437304P	P	20021231
US 2002-437403P	P	20021231
US 2002-437415P	P	20021231
US 2002-437487P	P	20021231
US 2003-463804P	P	20030418
US 2003-746460	A	20031224
WO 2003-US41449	W	20031226

OS MARPAT 141:140433

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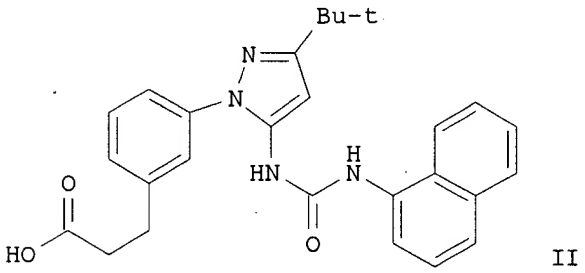

II

AB Title compds. (R1Xj)mA(NH)pLn(NH)pDEqYtQ [I; wherein R1 = (un)substituted (hetero)aryl; X, Y = independently O, S, NR6, NR6SO2, NR6CO, alkynyl, alkenyl, alkylene, O(CH2)h, NR6(CH2)h, wherein for each alkylene, O(CH2)h, and NR6(CH2)h, one of the methylene groups may be substituted with CO; h = 1-4; A = (un)substituted aryl, hetero(bi)cyclyl; D = (un)substituted Ph, pyrazolyl, pyrrolyl, imidazolyl, oxazolyl, thiazolyl, furyl, pyridyl, pyrimidyl; E = (un)substituted Ph, pyridinyl, pyrimidinyl; L = CO, SO2; j, m, n, p, q, t = independently 0, 1; Q = (un)substituted heterocyclyl, Ph, etc.; R6 = independently H, alkyl, allyl, TMS(CH2)2; with exceptions] were prepared as **p38** MAP kinase inhibitors. In a preferred embodiment, modulation of the activation state of **p38** kinase protein comprises the step of contacting the α-C helix, the α-D helix, the catalytic loop, the switch control ligand sequence, or the C-lobe residues of the kinase protein with I (no data). For example, hydrogenation of 3-(3-aminophenyl)acrylic acid Me ester using 10% Pd/C in EtOH provided the propionate, which was treated with NaNO2 in the presence of 6N HCl and SnCl2•2H2O to give the hydrazine. Reaction of the hydrazine with 4,4-dimethyl-3-oxopentanenitrile in EtOH and 6N HCl afforded Me 3-[3-(3-tert-butyl-5-amino-1H-pyrazole-1-yl)phenyl]propionate. Coupling of the amine with 1-naphthyl isocyanate in CH2Cl2, followed by reduction with LiOH in THF/MeOH/H2O provided the urea II. In a competition assay with SKF 86002 as a fluorescent probe, the latter inhibited **p38** MAP kinase with IC50 of 45 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of a wide variety of inflammatory conditions (no data).

L17 ANSWER 55 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:142968 HCAPLUS

DN 140:193056
TI Combinations of active agents with **p38** MAP kinase inhibitors, pharmaceutical compositions, and use in the treatment of cytokine-mediated diseases
IN Simianer, Stefan; Bilbault, Pascal; Cappola, Michael L.; Way, Susan Lynn
PA Boehringer Ingelheim Pharmaceuticals, Inc., USA; Boehringer Ingelheim France
SO PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004014387	A1	20040219	WO 2003-US25341	20030812
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004110755	A1	20040610	US 2003-638702	20030811
	CA 2497448	AA	20040219	CA 2003-2497448	20030812
	EP 1530477	A1	20050518	EP 2003-785255	20030812
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-403115P	P	20020813		
	WO 2003-US25341	W	20030812		

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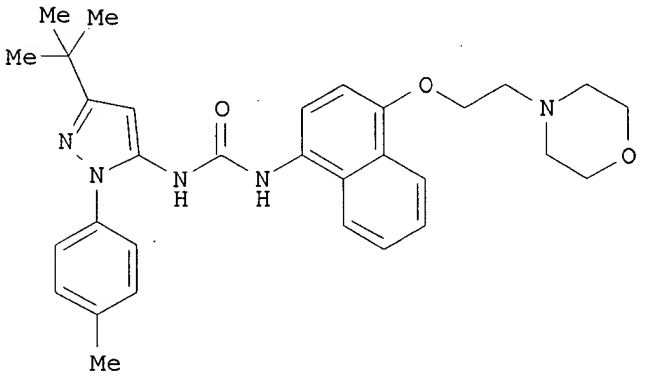


I

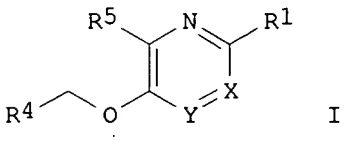
AB The invention relates to pharmaceutical combination therapies based on **p38** kinase inhibitors and another active ingredients, pharmaceutical compns. comprising such combinations, processes for preparing them, and their use in the treatment of cytokine-mediated diseases. Preparation of I (BIRB 796 BS) is described.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 56 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:41269 HCAPLUS
DN 140:77038
TI Preparation of 3-[heteroarylmethoxy]pyridines and their analogues as **p38** map kinase inhibitors
IN Murray, Christopher William; Hartshorn, Michael John; Frederickson, Martyn; Congreve, Miles Stuart; Padova, Alessandro; Woodhead, Steven John; Gill, Adrian Liam; Woodhead, Andrew James

PA Astex Technology Limited, UK
SO PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004004720	A1	20040115	WO 2003-GB2864	20030703
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1545523	A1	20050629	EP 2003-762777	20030703
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	GB 2002-15383	A	20020703		
	US 2002-393121P	P	20020703		
	GB 2002-26149	A	20021108		
	WO 2003-GB2864	W	20030703		

OS MARPAT 140:77038
GI



I

AB Title compds. I [X=Y = CR2=CR3, CR2=N; R1 = H, halo, amino, etc.; R2-3 = H, alkyl, aryl, etc.; R4 = carboaryl, heteroaryl; R5 = halo, amino, carboxamido, etc.] are prepared For instance, 2-amino-3-benzyloxypyridine is prepared by alkylation of 2-amino-3-hydroxypyridine with benzyl chloride. A related example, 2-amino-3-[2-phenylbenzyloxy]pyridine has IC50 < 10μM for **p38** map kinase. I are useful in the treatment of diseases ameliorated by inhibiting **p38** MAP kinase.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 57 OF 119 USPATFULL on STN
AN 2004:299960 USPATFULL
TI Novel cyanopyridine derivatives useful in the treatment of cancer and other disorders
IN Scott, William J., Guilford, CT, UNITED STATES
Dumas, Jacques, Bethany, CT, UNITED STATES
Boyer, Stephen, Hilden, GERMANY, FEDERAL REPUBLIC OF
Lee, Wendy, Hamden, CT, UNITED STATES
Chen, Yuanwei, North Haven, CT, UNITED STATES
Phillips, Barton, New Haven, CT, UNITED STATES
Verma, Sharad, New Haven, CT, UNITED STATES
Chen, Jianqing, New Haven, CT, UNITED STATES
Chen, Zhi, Hamden, CT, UNITED STATES
Fan, Jianmei, Hamden, CT, UNITED STATES
Raudenbush, Brian, Charlton, MA, UNITED STATES
Redman, Aniko, Derby, CT, UNITED STATES
Yi, Lin, Milford, CT, UNITED STATES
Zhu, Qingming, West Haven, CT, UNITED STATES
Adnane, Lila, Madison, CT, UNITED STATES
PI US 2004235829 A1 20041125

AI US 2004-788029 A1 20040227 (10)
PRAI US 2003-450323P 20030228 (60)
US 2003-450324P 20030228 (60)
US 2003-450348P 20030228 (60)
DT Utility
FS APPLICATION
LREP MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201
CLMN Number of Claims: 63
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2828
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to novel diaryl ureas, pharmaceutical compositions containing such compounds and the use of those compounds or compositions for treating hyper-proliferative and angiogenesis disorders, as a sole agent or in combination with cytotoxic therapies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 58 OF 119 USPATFULL on STN
AN 2004:292848 USPATFULL
TI Substituted pyridine derivatives useful in the treatment of cancer and other disorders
IN Dumas, Jacques, Bethany, CT, UNITED STATES
Lee, Wendy, Hamden, CT, UNITED STATES
Chen, Yuanwei, North Haven, CT, UNITED STATES
Adnane, Lila, Madison, CT, UNITED STATES
Scott, William J., Guilford, CT, UNITED STATES
Verma, Sharad, New Haven, CT, UNITED STATES
Chen, Jianqing, New Haven, CT, UNITED STATES
Chen, Zhi, Hamden, CT, UNITED STATES
Yi, Lin, Milford, CT, UNITED STATES
PI US 2004229937 A1 20041118
AI US 2004-789446 A1 20040301 (10)
PRAI US 2003-450323P 20030228 (60)
US 2003-450324P 20030228 (60)
US 2003-450348P 20030228 (60)
DT Utility
FS APPLICATION
LREP MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2564
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to novel diaryl ureas, pharmaceutical compositions containing such compounds and the use of those compounds or compositions for treating hyper-proliferative and angiogenesis disorders, as a sole agent or in combination with cytotoxic therapies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 59 OF 119 USPATFULL on STN
AN 2004:197419 USPATFULL
TI Methods of treating cancer
IN Moss, Neil, Ridgefield, CT, UNITED STATES
Regan, John Robinson, Larchmont, NY, UNITED STATES
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, UNITED STATES (U.S. corporation)
PI US 2004152725 A1 20040805
AI US 2004-761913 A1 20040120 (10)
RLI Division of Ser. No. US 2002-187942, filed on 1 Jul 2002, PENDING
PRAI US 2001-304511P 20010711 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368,

RIDGEFIELD, CT, 06877
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2900
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are methods of treating certain cytokine mediated diseases or conditions using novel aromatic heterocyclic compounds of the formula(I) wherein Ar.sub.1, Ar.sub.2, L, Q and X are described herein. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 60 OF 119 USPATFULL on STN
AN 2004:179046 USPATFULL
TI Process for the preparation of an essentially pure polymorph of an n-pyrazolyl-n'-naphthyl-urea
IN Samstag, Wendelin, Bad Kreuznach, GERMANY, FEDERAL REPUBLIC OF
Koch, Gunter, Schwabenheim, GERMANY, FEDERAL REPUBLIC OF
PA Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)
PI US 2004138216 A1 20040715
AI US 2003-727214 A1 20031203 (10)
PRAI US 2002-436136P 20021223 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P. O. BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 406
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are improved processes for the preparation of a polymorph of 1-[tert-butyl-1-p-tolyl-1H-pyrazol-5-yl]-3-[4-(2-morpolinin-4-yl-ethoxy)naphthalen-1-yl]-urea (1) by crystallization from an alcohol, wherein the improvement is that crude (1) is treated with ethanol.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 61 OF 119 USPATFULL on STN
AN 2004:145082 USPATFULL
TI Combination therapy with **p38** MAP kinase inhibitors and their pharmaceutical compositions
IN Simianer, Stefan, Mittelbiberach, GERMANY, FEDERAL REPUBLIC OF
Bilbault, Pascal, Reims, FRANCE
Cappola, Michael L., Wilton, CT, UNITED STATES
Way, Susan Lynn, Danbury, CT, UNITED STATES
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT (non-U.S. corporation)
Boehringer Ingelheim France, Paris, FRANCE (non-U.S. corporation)
PI US 2004110755 A1 20040610
AI US 2003-638702 A1 20030811 (10)
PRAI US 2002-403115P 20020813 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4651
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to pharmaceutical combinations therapies based on **p38** kinase inhibitors and another active ingredient, pharmaceutical compositions comprising such combinations, processes for preparing them and their use in the treatment of cytokine mediated diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 62 OF 119 USPATFULL on STN
AN 2004:31819 USPATFULL
TI Aryl ureas with raf kinase and angiogenisis inhibiting activity
IN Dumas, Jacques, Bethany, CT, UNITED STATES
Scott, William J., Guilford, CT, UNITED STATES
Elting, James, Madison, CT, UNITED STATES
Hatoum-Makdad, Holia, Hamden, CT, UNITED STATES
PA BAYER CORPORATION, Pittsburgh, PA (U.S. corporation)
PI US 2004023961 A1 20040205
AI US 2003-361844 A1 20030211 (10)
PRAI US 2002-354948P 20020211 (60)
DT Utility
FS APPLICATION
LREP MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4402
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to methods of using aryl ureas to treat diseases mediated by raf kinase and diseases mediated by the VEGF induced signal transduction pathway characterized by abnormal angiogenesis or hyperpermeability processes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 63 OF 119 USPATFULL on STN
AN 2004:25196 USPATFULL
TI Compounds useful as anti-inflammatory agents
IN Cirillo, Pier F., Woodbury, CT, UNITED STATES
Breitfelder, Steffen, Assmannshardt, GERMANY, FEDERAL REPUBLIC OF
Patel, Usha R., Brookfield, CT, UNITED STATES
Proudfoot, John Robert, Newtown, CT, UNITED STATES
Swinamer, Alan D., Bethel, CT, UNITED STATES
Takahashi, Hidenori, LaGrangeville, NY, UNITED STATES
Gilmore, Thomas A., Cambridge, MA, UNITED STATES
Sharma, Rajiv, Foster City, CA, UNITED STATES
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, UNITED STATES, 06877-0368 (U.S. corporation)
PI US 2004019038 A1 20040129
AI US 2003-624289 A1 20030721 (10)
RLI Division of Ser. No. US 2001-962709, filed on 25 Sep 2001, GRANTED, Pat. No. US 6660732 Division of Ser. No. US 2000-505582, filed on 16 Feb 2000, GRANTED, Pat. No. US 6358945
PRAI US 1999-124148P 19990312 (60)
US 1999-165867P 19991116 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 6759
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel aromatic compounds which are useful for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are pharmaceutical compositions containing and processes of making such compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 64 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:690875 HCAPLUS
DN 141:345501

TI Discovery and Characterization of a Substrate Selective **p38** α Inhibitor

AU Davidson, Walter; Frego, Lee; Peet, Gregory W.; Kroe, Rachel R.; Labadia, Mark E.; Lukas, Susan M.; Snow, Roger J.; Jakes, Scott; Grygon, Christine A.; Pargellis, Christopher; Werneburg, Brian G.

CS Department of Immunology and Inflammation, Research and Development Center, Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, 06877, USA

SO Biochemistry (2004), 43(37), 11658-11671
CODEN: BICHAW; ISSN: 0006-2960

PB American Chemical Society

DT Journal

LA English

AB A novel inhibitor of **p38** mitogen-activated protein kinase (**p38**), CMPD1, identified by high-throughput screening, is characterized herein. Unlike the **p38** inhibitors described previously, this inhibitor is substrate selective and noncompetitive with ATP. In steady-state kinetics expts., CMPD1 was observed to prevent the **p38**.alpha.-dependent phosphorylation (Kiapp = 330 nM) of the splice variant of mitogen-activated protein kinase-activated protein kinase 2 (MK2a) that contains a docking domain for **p38**.alpha. and **p38**.beta., but it did not prevent the phosphorylation of ATF-2 (Kiapp > 20 μM). In addition to kinetic studies, isothermal titration calorimetry and surface plasmon resonance expts. were performed to elucidate the mechanism of inhibition. While isothermal titration calorimetry anal. indicated that CMPD1 binds to **p38**.alpha., CMPD1 was not observed to compete with ATP for **p38**.alpha., nor was it able to interrupt the binding of **p38**.alpha. to MK2a observed by surface plasmon resonance. Therefore, deuterium exchange mass spectrometry (DXMS) was employed to study the **p38** α·CMPD1 inhibitory complex, to provide new insight into the mechanism of substrate selective inhibition. The DXMS data obtained for the **p38**.alpha.·CMPD1 complex were compared to the data obtained for the **p38**.alpha.·MK2a complex and a **p38**.alpha.·active site binding inhibitor complex. Alterations in the DXMS behavior of both **p38**.alpha. and MK2a were observed upon complex formation, including but not limited to the interaction between the carboxy-terminal docking domain of MK2a and its binding groove on **p38**.alpha.. Alterations in the D2O exchange of **p38**.alpha. produced by CMPD1 suggest that the substrate selective inhibitor binds in the vicinity of the active site of **p38**.alpha., resulting in perturbations to regions containing nucleotide binding pocket residues, docking groove residues (E160 and D161), and a Mg2+ ion cofactor binding residue (D168). Although the exact mechanism of substrate selective inhibition by this novel inhibitor has not yet been disclosed, the results suggest that CMPD1 binding in the active site region of **p38**.alpha. induces perturbations that may result in the suboptimal positioning of substrates and cofactors in the transition state, resulting in selective inhibition of **p38** α activity.

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 65 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:267661 HCAPLUS

DN 140:417262

TI General Model for Estimation of the Inhibition of Protein Kinases Using Monte Carlo Simulations

AU Tominaga, Yukio; Jorgensen, William L.

CS Department of Chemistry, Yale University, New Haven, CT, 06520-8107, USA

SO Journal of Medicinal Chemistry (2004), 47(10), 2534-2549
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

AB Monte Carlo statistical mechanics simulations were used in combination with the extended linear response (ELR) approach to develop a model to predict the activities of kinase inhibitors. One hundred forty eight inhibitors of three protein kinases, cyclin-dependent kinase 2 (CDK2),

lymphocyte-specific kinase (Lck), and **p38** mitogen-activated protein kinase were considered. The inhibitor sets for the individual kinases were analyzed first, and ELR models using only three descriptors were obtained with correlation coeffs., r2, of 0.7-0.8. Models for each pair of kinases were then developed and used to predict the activities of the inhibitors for the remaining kinase with resultant q2 values of 0.71 (CDK2), 0.70 (Lck), and 0.54 (**p38**). Finally, the three datasets were combined to yield a general ELR model for kinase inhibition; with just three phys. reasonable descriptors, EXX, ΔHBtotal, and ΔSASA, the r2 and leave-one-out q2 are 0.69 and 0.67. The optimization of the model was confirmed using a genetic algorithm. The descriptors reflect the structural requirements for strong inhibition: good steric and electrostatic complementarities between inhibitor and protein, limited loss of hydrogen bonds for the inhibitor upon binding, and increased burial of surface area of the inhibitor.

RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 66 OF 119 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2004:397560 BIOSIS
DN PREV200400400342
TI Biologics in **inflammatory bowel disease**: how much progress have we made?.
AU Sandborn, W.J. [Reprint Author]; Faubion, W. A.
CS Div Gastroenterol and Hepatol, Mayo Clin and Mayo Fdn, 200 1st St SW, Rochester, MN, 55905, USA
sandborn.william@mayo.edu
SO Gut, (September 2004) Vol. 53, No. 9, pp. 1366-1373. print.
ISSN: 0017-5749 (ISSN print).
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 13 Oct 2004
Last Updated on STN: 13 Oct 2004

L17 ANSWER 67 OF 119 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 9
AN 2005:76959 BIOSIS
DN PREV200500078531
TI Synthesis of deuterium, tritium, and carbon-14 labeled BIRB 796, a **p38** MAP kinase inhibitor.
AU Latli, Bachir [Reprint Author]
CS Ctr Res and DevDept Med Chem, Boehringer Ingelheim Pharmaceut Inc, 900 Ridgebury Rd, Ridgefield, CT, 06877, USA
blatli@rdg.boehringer-ingelheim.com
SO Journal of Labelled Compounds and Radiopharmaceuticals, (October 30 2004) Vol. 47, No. 12, pp. 847-856. print.
ISSN: 0362-4803 (ISSN print).
DT Article
LA English
ED Entered STN: 23 Feb 2005
Last Updated on STN: 23 Feb 2005
AB 1-(5-tert-Butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-(4-(2-morpholin-4-yl-ethoxy)naphthalen-1-yl)urea (BIRB 796), currently in clinical trials for the treatment of inflammatory diseases, is a potent inhibitor of **p38** MAP kinase. Labeled BIRB 796 with stable and radioactive isotopes was required for metabolism, distribution, and absorption studies. We first report the synthesis of carbon-14 labeled BIRB 796 with a specific activity of 2 GBq/mmol (54.2 mCi/mmol), using (14C)-phosgene under modified Schotten-Baumann conditions; second the preparation of tritium-labeled BIRB 796 with a specific activity of 659 GBq/mmol (17.81 Ci/mmol) by reductive dehalogenation of iodo-BIRB 796 with tritium gas; and finally, the synthesis of2 H8-BIRB 796 using morpholine-2,2,3,3,5,5,6,6-2H8 with isotopic enrichment of 98.9 at %2 H. Copyright Copyright 2004 John Wiley & Sons, Ltd.

L17 ANSWER 68 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:839017 HCAPLUS
DN 142:311699
TI Structural insights into the conformational selectivity of STI-571 and related kinase inhibitors
AU Mol, Clifford D.; Fabbro, Doriano; Hosfield, David J.
CS Syrrx Inc, La Jolla, CA, 92121, USA
SO Current Opinion in Drug Discovery & Development (2004), 7(5), 639-648
CODEN: CODDFF; ISSN: 1367-6733
PB Thomson Scientific
DT Journal; General Review
LA English
AB A review. STI-571 (Gleevec) is a highly successful cancer drug due to its activity as an inhibitor of the Abelson cytoplasmic tyrosine kinase (Abl), which is constitutively active in a majority of patients with chronic myelogenous leukemia. STI-571 also inhibits two type III receptor tyrosine kinases, c-Kit and platelet-derived growth factor receptor, and functions by targeting inactive conformations of these kinases. This review focuses on recent developments in x-ray co-crystal structure analyses of STI-571 bound to Abl and the c-Kit receptor tyrosine kinase domain, and also three other relevant kinase inhibitor co-crystal structures. The similar structural features of these inactive kinases suggest they will be useful for the successful drug discovery and development of specific and targeted gene-based cancer drugs.
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 69 OF 119 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2005:114669 BIOSIS
DN PREV200500112085
TI Fragment based discovery of inhibitors of **p38** kinase.
AU Davis, Deborah; Curry, Jayne; Gill, Adrian; Vincovic, Mladen; Jhoti, Harren
SO Biochemical Society Transactions, (August 2004) Vol. 32, No. Part 4, pp. 167A. print.
Meeting Info.: BioScience2004: From Molecules to Organisms. Glasgow, UK. July 18-22, 2004. The Biochemical Society.
CODEN: BCSTB5. ISSN: 0300-5127.
DT Conference; (Meeting)
Conference; (Meeting Poster)
LA English
ED Entered STN: 23 Mar 2005
Last Updated on STN: 23 Mar 2005

L17 ANSWER 70 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:262323 HCAPLUS
DN 141:116347
TI Nuclear Export Inhibitors and Kinase Inhibitors Identified Using a MAPK-Activated Protein Kinase 2 Redistribution Screen
AU Almholt, Dorthe L. C.; Loechel, Frosty; Nielsen, Soren J.; Krog-Jensen, Christian; Terry, Robert; Bjorn, Sara P.; Pedersen, Hans C.; Praestegaard, Morten; Moller, Soren; Heide, Morten; Pagliaro, Len; Mason, Anthony J.; Butcher, Steven; Dahl, Soren W.
CS BioImage A/S, Soborg, Den.
SO Assay and Drug Development Technologies (2004), 2(1), 7-20
CODEN: ADDTAR; ISSN: 1540-658X
PB Mary Ann Liebert, Inc.
DT Journal
LA English
AB Redistribution (BioImage A/S, Soborg, Denmark) is a novel high-throughput screening technol. that monitors translocation of specific protein components of intracellular signaling pathways within intact mammalian cells, using green fluorescent protein as a tag. A single Redistribution assay can be used to identify multiple classes of compds. that act at, or upstream of, the level of the protein target used in the primary screening assay. Such compds. may include both conventional and allosteric enzyme inhibitors, as well as protein-protein interaction modulators. We have developed a series of Redistribution assays to discover and characterize

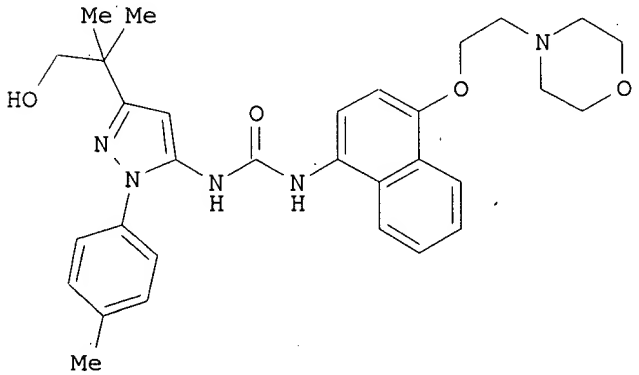
compds. that inhibit tumor necrosis factor-α biosynthesis via modulation of the **p38** mitogen-activated protein kinase (MAPK) pathway. A primary assay was designed to identify low-mol.-weight compds. that inhibit the activation-dependent nuclear export of the **p38** kinase substrate MAPK-activated protein kinase 2 (MK2). Hits from the primary screen were categorized, using secondary assays, either as direct inhibitors of MK2 nuclear export, or as inhibitors of the upstream **p38** MAPK pathway. Activity profiles are presented for a nuclear export inhibitor, and a compound that structurally and functionally resembles a known **p38** kinase inhibitor. These results demonstrate the utility of Redistribution technol. as a pathway screening method for the identification of diverse and novel compds. that are active within therapeutically important signaling pathways.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 71 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 10
AN 2003:150529 HCAPLUS
DN 138:205052
TI Preparation of 1-(pyrazol-3-yl)-3-(1-naphthyl)ureas as antiinflammatory agents
IN Cirillo, Pier Francesco; Dinallo, Roger; Regan, John Robinson; Riska, Paul S.; Swinamer, Alan David; Tan, Zhulin; Walter, Brian Andrew
PA Boehringer Ingelheim Pharmaceuticals, Inc., USA
SO U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 879,776, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6525046	B1	20030225	US 2002-165372	20020607
	US 6319921	B1	20011120	US 2000-484638	20000118
	US 6333325	B1	20011225	US 2001-871559	20010531
	US 2002058678	A1	20020516	US 2001-879776	20010612
	US 6329415	B1	20011211	US 2001-891579	20010626
	US 2002065285	A1	20020530	US 2001-891820	20010626
	US 6506748	B2	20030114		
PRAI	US 2000-484638	A3	20000118		
	US 2001-879776	B2	20010612		
	US 1999-116400P	P	19990119		

OS MARPAT 138:205052
GI



I

AB The title compds. Ar1NHC(:X)NHAr2LQ [Ar1 = pyrazolyl, pyrrolyl, imidazolyl, etc.; Ar2 = Ph, naphthyl, quinolyl, etc.; L = alkylene wherein one or more methylene groups are optionally replaced by O, N or S; Q = Ph, naphthyl, pyridyl, etc.; X = O, S], useful for treating diseases involving

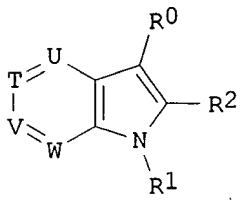
inflammation such as chronic inflammatory diseases, were prepared E.g., a multi-step synthesis of I, starting from Me 2,2-dimethyl-3-hydroxypropionate, was given. Representative title ureas showed IC50 of < 10 μM against TNF production in THP cells.

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 72 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:837074 HCAPLUS
DN 139:337981
TI Preparation of indoles as **p38** MAP kinase inhibitors
IN Frederickson, Martyn; Gill, Adrian Liam; Padova, Alessandro; Congreve, Miles Stuart
PA Astex Technology Limited, UK
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003087087	A2	20031023	WO 2003-GB1507	20030408
	WO 2003087087	A3	20031218		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1495016	A2	20050112	EP 2003-720680	20030408
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005526831	T2	20050908	JP 2003-584043	20030408
	US 2005124620	A1	20050609	US 2004-962085	20041008
PRAI	GB 2002-8248	A	20020409		
	GB 2002-15180	A	20020629		
	WO 2003-GB1507	W	20030408		

OS MARPAT 139:337981
GI



I

AB The title compds. [I; U, T, V and W are each a N atom or CR4 provided that no more than three of U, T, V and W are N atoms; R0 = H, alkyl, halo, AR3; R1 = H, alkyl, AR3; provided that only one of R0 and R1 = AR3; R2 = H, alkyl, halo; A = carbon- or heteroatom-containing linker group having a linking chain length of one or two atoms; R3 = 5-12 membered monocyclic or bicyclic heteroaryl; R4 = H, OH, halo, NO2, CN, etc.; with the provisos], useful for use in the prophylaxis or treatment of a disease state or condition mediated by a **p38** MAP kinase such as **rheumatoid** arthritis and **osteoarthritis**, were prepared and formulated. Thus, reacting 4-vinylpyridine with 5-methylindole afforded I [U, V and W = CH; Y = CMe; R0 = 2-(4-pyridyl)ethyl; R1, R2 = H] which showed IC50 of 250 μM against **p38** MAP kinase.

L17 ANSWER 73 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:818288 HCAPLUS
DN 139:312463
TI New pharmaceutical compositions based on anticholinergics and **p38** kinase inhibitors
IN Jung, Birgit; Pairet, Michel; Pieper, Michael P.; Reiser, Hans Clemens
PA Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany; Boehringer Ingelheim Pharmaceuticals, Inc.
SO PCT Int. Appl., 191 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003084539	A2	20031016	WO 2003-EP3624	20030408
	WO 2003084539	A3	20040902		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003225089	A1	20031204	US 2003-408718	20030407
	CA 2479522	AA	20031016	CA 2003-2479522	20030408
	EP 1496900	A2	20050119	EP 2003-720433	20030408
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003009099	A	20050329	BR 2003-9099	20030408
	JP 2005529098	T2	20050929	JP 2003-581779	20030408
PRAI	US 2002-371514P	P	20020410		
	WO 2003-EP3624	W	20030408		

OS MARPAT 139:312463
AB The present invention relates to novel pharmaceutical compns. based on anticholinergics and **p38** kinase inhibitors, processes for preparing them and their use in the treatment of respiratory diseases. For example, inhalatable powders comprised tiotropium bromide (as anticholinergic) 10.8, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]urea (as **p38** kinase inhibitor) 3500, and lactose 3489.2 μg per capsule.

L17 ANSWER 74 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:818257 HCAPLUS
DN 139:312451
TI Inhalant **p38** kinase inhibitor formulations for treating mucus hypersecretion
IN Jung, Birgit
PA Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SO PCT Int. Appl., 191 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003084503	A2	20031016	WO 2003-EP3434	20030402
	WO 2003084503	A3	20040408		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003220336	A1	20031127	US 2003-400421	20030327
CA 2479520	AA	20031016	CA 2003-2479520	20030402
EP 1494645	A2	20050112	EP 2003-720407	20030402
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009009	A	20050322	BR 2003-9009	20030402
JP 2005528374	T2	20050922	JP 2003-581743	20030402
PRAI EP 2002-7699	A	20020405		
US 2002-385856P	P	20020605		
WO 2003-EP3434	W	20030402		

OS MARPAT 139:312451

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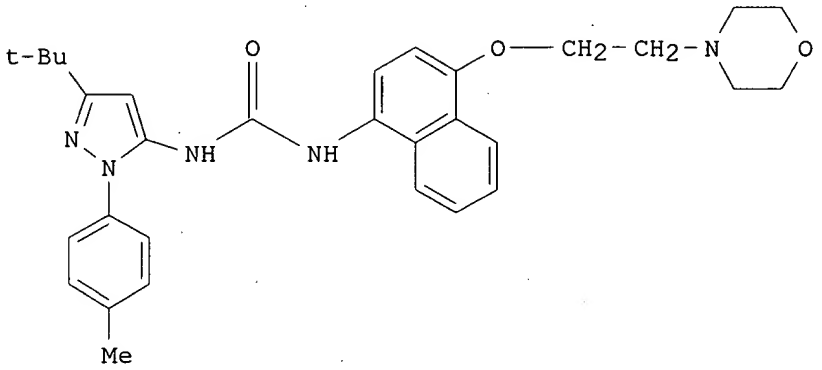

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AB The invention relates to the use of **p38** kinase inhibitors for the preparation of a pharmaceutical composition suitable for inhalation for the treatment of mucus hypersecretion. Furthermore the invention is directed to pharmaceutical compns. suitable for inhalation comprising **p38** kinase inhibitors such as I and methods for their preparation

L17 ANSWER 75 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:656575 HCAPLUS

DN 139:197476

TI Preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity

IN Dumas, Jacques; Scott, William J.; Elting, James; Hatoum-Makdad, Holia

PA Bayer Corporation, USA

SO PCT Int. Appl., 142 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003068223	A1	20030821	WO 2003-US4102	20030211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2004023961	A1	20040205	US 2003-361844	20030211
PRAI US 2002-354948P	P	20020211		

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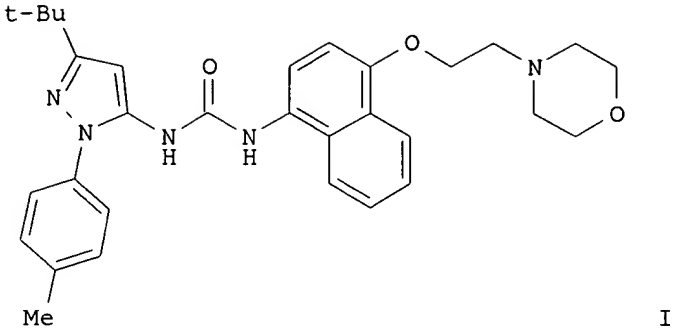

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AB 283 Of the title ureas useful for treating diseases mediated by raf kinase and diseases mediated by the VEGF induced signal transduction pathway characterized by abnormal angiogenesis or hyperpermeability processes, were claimed. Synthesis of 6 ureas such as I was described. Thus, reacting 3-(tert-butyl)-1-(4-methylphenyl)pyrazole-5-ylamine with 4-(2-morpholin-4-ylethoxy)naphthylamine (prepns. given) and CDI in CH2Cl2 afforded 80% I which showed IC50 of < 1 μM in in vitro raf kinase and in in vitro Flk-1 ELISA assay.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 76 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:472391 HCAPLUS
DN 139:30815
TI Method for administration of BIRB 796 BS for the treatment of human cytokine mediated diseases
IN Grob, Peter M.; Madwed, Jeffrey B.; Pargellis, Christopher; Yong, Chan Loi
PA Boehringer Ingelheim Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003049742	A1	20030619	WO 2002-US39289	20021206
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2465759	AA	20030619	CA 2002-2465759	20021206
	US 2003118575	A1	20030626	US 2002-313667	20021206
	EP 1455791	A1	20040915	EP 2002-804546	20021206
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2005511722	T2	20050428	JP 2003-550791	20021206
PRAI	US 2001-339249P	P	20011211		
	WO 2002-US39289	W	20021206		

AB Disclosed are methods of administration of BIRB 796 BS, a **p38** MAPK inhibitor, at particular dosages for the treatment of human cytokine mediated diseases.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 77 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:319714 HCAPLUS
DN 138:338157
TI Preparation of 1,4-disubstituted benzo-fused ureas as cytokine inhibitors
IN Cirillo, Pier F.; Hammach, Abdelhakim; Regan, John R.
PA Boehringer Ingelheim Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003032989	A1	20030424	WO 2002-US32809	20021011
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2462441	AA	20030424	CA 2002-2462441	20021011
	US 2003162968	A1	20030828	US 2002-269173	20021011
	US 6825184	B2	20041130		
	EP 1438048	A1	20040721	EP 2002-801703	20021011
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2005506350	T2	20050303	JP 2003-535792	20021011
PRAI	US 2001-330254P	P	20011018		
	WO 2002-US32809	W	20021011		

OS MARPAT 138:338157
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; ring A = fused (un)saturated ring containing 3-5 carbon atoms (wherein ring A or the Ph ring to which it is fused is optionally substituted); G = (un)substituted 5-membered heteroaryl; Q = (un)substituted naphthyl, benzocyclobutanyl, indanyl, etc.; X = O, S] which are active as anti-inflammatory agents, were prepared. Thus, reacting the carbamate II with the amine III (multi-step preparation given) in DMSO afforded 84% urea IV. The preferred compds. I including those from the synthetic examples were evaluated for their inhibition of TNFα production in THP cells, and showed IC50 < 10 μM.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 78 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:154285 HCAPLUS
DN 138:193302
TI Parenteral formulations of BIRB 796
IN Cappola, Michael L.; Way, Susan L.
PA Boehringer Ingelheim Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	WO 2003015828	A1	20030227	WO 2002-US25110	20020808
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2454913	AA	20030227	CA 2002-2454913	20020808
	US 2003068340	A1	20030410	US 2002-214782	20021021
PRAI	US 2001-313527P	P	20010820		
	WO 2002-US25110	W	20020808		

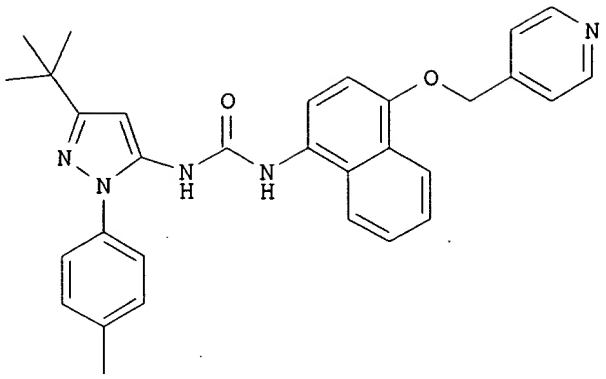
AB Preparation of improved parenteral dosage forms of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphth len-1-yl]-urea (BIRB 796), using an oligosaccharide capable of forming an association or complex with BIRB 796, e.g., a cyclodextrin, are described. Also disclosed are methods of treating cytokine-mediated diseases using such formulations and compns.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CÍTATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 79 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:57886 HCAPLUS
DN 138:122641
TI Method of treating cytokine mediated diseases using pyrazolylureas.
IN Moss, Neil; Regan, John R.
PA Boehringer Ingelheim Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003005999	A2	20030123	WO 2002-US20649	20020701
	WO 2003005999	A3	20030417		
	WO 2003005999	C1	20040422		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2453147	AA	20030123	CA 2002-2453147	20020701
	US 2003130309	A1	20030710	US 2002-187942	20020701
	US 6916814	B2	20050712		
	EP 1408950	A2	20040421	EP 2002-746764	20020701
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004536845	T2	20041209	JP 2003-511806	20020701
	US 2004152725	A1	20040805	US 2004-761913	20040120
PRAI	US 2001-304511P	P	20010711		
	US 2002-187942	A3	20020701		
	WO 2002-US20649	W	20020701		

OS MARPAT 138:122641
GI



I

AB A method of treating lung inflammation, endometriosis, behcet's disease, uveitis, ankylosing spondylitis, pancreatitis, cancer, percutaneous transluminal coronary angioplasty, alzheimer's disease, traumatic arthritis, **sepsis**, chronic obstructive pulmonary disease, and congestive heart failure comprises administration of Ar1NHC(:X)NHAr2LQ [Ar1 = (substituted) pyrrolyl, pyrrolidinyl, pyrazolyl, imidazolyl, oxazolyl, thiazolyl, furyl, thienyl; Ar2 = (substituted) Ph, naphthyl, quinolinyl, isoquinolinyl, tetrahydronaphthyl, tetrahydroisoquinolinyl, benzimidazolyl, benzofuryl, indanyl, indolyl, etc.; L = (O-, S-, or N-interrupted) (unsatd.) (substituted) alkylene; Q = (substituted) Ph, naphthyl, pyridyl, pyrimidinyl, imidazolyl, tetrahydropyranyl, tetrahydrofuryl, dioxanyl, alkoxy, amino, etc.; X = O, S]. Thus, 5-amino-3-tert-butyl-1-(4-methylphenyl)pyrazole was stirred with COCl2 and NaHCO3 in PhMe/CH2Cl2 at 0-5° for 15 min. The organic residue was stirred overnight with 1-amino-4-(4-pyridinylmethoxy)naphthalene dihydrochloride (preparation given) and diisopropylethylamine in THF to give title compound (I). Representative title compds. inhibited TNF production in THP cells with IC50<10 μM.

L17 ANSWER 80 OF 119 USPATFULL on STN
AN 2003:330650 USPATFULL
TI 1,4-Benzofused urea compounds useful in treating cytokine mediated diseases
IN Cirillo, Pier Francesco, Woodbury, CT, UNITED STATES
Hammach, Abdelhakim, Danbury, CT, UNITED STATES
Regan, John Robinson, Larchmont, NY, UNITED STATES
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, 06877-0368 (U.S. corporation)
PI US 2003232865 A1 20031218
AI US 2003-369847 A1 20030219 (10)
PRAI US 2002-359809P 20020225 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2439
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are 1,4-disubstituted benzo-fused urea compounds of formula (I): ##STR1##

wherein Ar, X, A, L, and Q of formula(I) are defined herein. The compounds inhibit production of cytokines involved in inflammatory processes and are thus useful for treating diseases and pathological conditions involving inflammation such as chronic inflammatory disease. Also disclosed are processes for preparing these compounds and pharmaceutical compositions comprising these compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 81 OF 119 USPATFULL on STN
AN 2003:319340 USPATFULL
TI Pharmaceutical compositions based on anticholinergics and **p38** kinase inhibitors
IN Jung, Birgit, Laupheim, GERMANY, FEDERAL REPUBLIC OF
Pairet, Michel, Biberach, GERMANY, FEDERAL REPUBLIC OF
Pieper, Michael P., Biberach, GERMANY, FEDERAL REPUBLIC OF
Reiser, Hans Clemens, New York, NY, UNITED STATES
PA Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)
PI US 2003225089 A1 20031204
AI US 2003-408718 A1 20030407 (10)
PRAI US 2002-371514P 20020410 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P. O. BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 31
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 6684
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel pharmaceutical compositions based on anticholinergics and **p38** kinase inhibitors, processes for preparing them and their use in the treatment of respiratory diseases.,

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 82 OF 119 USPATFULL on STN
AN 2003:319328 USPATFULL
TI Intermediate arylamine compounds
IN Cirillo, Pier F., Woodbury, CT, UNITED STATES
Breitfelder, Steffen, Ridgefield, CT, UNITED STATES
Patel, Usha R., Brookfield, CT, UNITED STATES
Proudfoot, John R., Newtown, CT, UNITED STATES
Swinamer, Alan D., Danbury, CT, UNITED STATES
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT (U.S. corporation)
PI US 2003225077 A1 20031204
AI US 2003-424613 A1 20030428 (10)
RLI Continuation of Ser. No. US 2001-962057, filed on 25 Sep 2001, PENDING
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5832
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel aromatic compounds which are useful for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are and pharmaceutical compositions containing, intermediate compounds and processes of making such compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 83 OF 119 USPATFULL on STN
AN 2003:312731 USPATFULL
TI Method of treating mucus hypersecretion
IN Jung, Birgit, Laupheim, GERMANY, FEDERAL REPUBLIC OF
PA Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)
PI US 2003220336 A1 20031127
AI US 2003-400421 A1 20030327 (10)
PRAI EP 2002-7699 20020405

US 2002-385856P 20020605 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P. O. BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 6938
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to the use of **p38** kinase inhibitors for the preparation of a pharmaceutical composition suitable for inhalation for the treatment of mucus hypersecretion. Furthermore the invention is directed to pharmaceutical compositions suitable for inhalation comprising **p38** kinase inhibitors and to methods for the preparation thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 84 OF 119 USPATFULL on STN
AN 2003:232767 USPATFULL
TI 1,4-Disubstituted benzo-fused urea compounds
IN Cirillo, Pier Francesco, Woodbury, CT, UNITED STATES
Hammach, Abdelhakim, Danbury, CT, UNITED STATES
Regan, John R., Larchmont, NY, UNITED STATES
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT (U.S. corporation)
PI US 2003162968 A1 20030828
US 6825184 B2 20041130
AI US 2002-269173 A1 20021011 (10)
PRAI US 2001-330254P 20011018 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2450
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are compounds of the formulas (I) & (II) shown below which are active as anti-inflammatory agents. Also disclosed are methods of using and making such compounds. ##STR1##

wherein G, X, A and Q are described herein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 85 OF 119 USPATFULL on STN
AN 2003:188516 USPATFULL
TI Methods of treating cytokine mediated diseases
IN Moss, Neil, Ridgefield, CT, UNITED STATES
Regan, John Robinson, Larchmont, NY, UNITED STATES
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT (U.S. corporation)
PI US 2003130309 A1 20030710
US 6916814 B2 20050712
AI US 2002-187942 A1 20020701 (10)
PRAI US 2001-304511P 20010711 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2954
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are methods of treating certain cytokine mediated diseases or conditions using novel aromatic heterocyclic compounds of the formula(I) wherein Ar.sub.1,Ar.sub.2,L,Q and X are described herein. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 86 OF 119 USPATFULL on STN
AN 2003:172731 USPATFULL
TI Method for administering BIRB 796 BS
IN Grob, Peter M., New Fairfield, CT, UNITED STATES
Madwed, Jeffrey B., Trumbull, CT, UNITED STATES
Pargellis, Christopher, West Redding, CT, UNITED STATES
Yong, Chan Loi, Brookfield, CT, UNITED STATES
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT (U.S. corporation)
PI US 2003118575 A1 20030626
AI US 2002-313667 A1 20021206 (10)
PRAI US 2001-339249P 20011211 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)
LN.CNT 409
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are methods of administering BIRB 796 BS, a **p38** MAPK inhibitor, at particular dosages.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 87 OF 119 USPATFULL on STN
AN 2003:133551 USPATFULL
TI Methods for coating pharmaceutical core tablets
IN Cappola, Michael, Wilton, CT, UNITED STATES
Gereg, George W., Bethel, CT, UNITED STATES
Way, Susan, Danbury, CT, UNITED STATES
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT (U.S. corporation)
PI US 2003091636 A1 20030515
US 6808721 B2 20041026
AI US 2002-282383 A1 20021029 (10)
RLI Division of Ser. No. US 2001-902822, filed on 11 Jul 2001, PENDING
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 649
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A formulation comprising, and process for preparing, improved oral dosage forms of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea, a chemical entity with anti-inflammatory properties. Granulation of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea within specified ranges provides improved dissolution of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea and oral bioavailability, as well as content uniformity. Incorporation into the formulation of an aqueous soluble inclusion compound capable of forming a complex with 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea, such as beta-cyclodextrin provides enhanced stability of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea, in particular in highly ionic environments. Chipping and disintegration of tablets containing

more than about 10% betacyclodextrin can be prevented by applying a polymeric coat to the surface of the tablet at a temperature below 40° C.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 88 OF 119 USPATFULL on STN
AN 2003:99236 USPATFULL
TI Parenteral formulations of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea
IN Cappola, Michael L., Wilton, CT, UNITED STATES
Way, Susan Lynn, Danbury, CT, UNITED STATES
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, UNITED STATES (U.S. corporation)
PI US 2003068340 A1 20030410
AI US 2002-214782 A1 20021021 (10)
PRAI US 2001-313527P 20010820 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 499
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are formulations and compositions comprising, and process for preparing, improved parenteral dosage forms of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea. Also disclosed are methods of treating cytokine mediated diseases using such formulations and compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 89 OF 119 USPATFULL on STN
AN 2003:11164 USPATFULL
TI Compounds useful as anti-inflammatory agents
IN Francesco Cirillo, Pier, Woodbury, CT, UNITED STATES
Goldberg, Daniel R., Redding, CT, UNITED STATES
Hammach, Abdelhakim, Danbury, CT, UNITED STATES
Moss, Neil, Ridgefield, CT, UNITED STATES
Regan, John Robinson, Larchmont, NY, UNITED STATES
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, UNITED STATES (U.S. corporation)
PI US 2003008868 A1 20030109
US 6852717 B2 20050208
AI US 2002-143322 A1 20020510 (10)
PRAI US 2001-291425P 20010516 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1260
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are compounds useful in pharmaceutic compositions for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are processes of making such compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 90 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:738975 HCAPLUS
DN 139:301299
TI Structure-Activity Relationships of the **p38**.alpha. MAP Kinase

Inhibitor 1-(5-tert-Butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)naph- thalen-1-yl]urea (BIRB 796)
AU Regan, John; Capolino, Alison; Cirillo, Pier F.; Gilmore, Thomas; Graham, Anne G.; Hickey, Eugene; Kroe, Rachel R.; Madwed, Jeffrey; Moriak, Monica; Nelson, Richard; Pargellis, Christopher A.; Swinamer, Alan; Torcellini, Carol; Tsang, Michele; Moss, Neil
CS Department of Medicinal Chemistry, Boehringer Ingelheim Pharmaceuticals Research and Development Center, Ridgefield, CT, 06877, USA
SO Journal of Medicinal Chemistry (2003), 46(22), 4676-4686
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 139:301299
AB We report on the structure-activity relationships (SAR) of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)naphthalen-1-yl]urea (BIRB 796), an inhibitor of **p38** α MAP kinase which has advanced into human clin. trials for the treatment of autoimmune diseases. Thermal denaturation was used to establish mol. binding affinities for this class of **p38**.alpha. inhibitors. The tert-Bu group remains a critical binding element by occupying a lipophilic domain in the kinase which is exposed upon rearrangement of the activation loop. An aromatic ring attached to N-2 of the pyrazole nucleus provides important π-CH2 interactions with the kinase. The role of groups attached through an ethoxy group to the 4-position of the naphthalene and directed into the ATP-binding domain is elucidated. Pharmacophores with good hydrogen bonding potential, such as morpholine, pyridine, and imidazole, shift the melting temperature of **p38**.alpha. by 16-17° translating into Kd values of 50-100 pM. Finally, we describe several compds. that potently inhibit TNF-α production when dosed orally in mice.
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 91 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:738972 HCAPLUS
DN 139:374260
TI Thermal Denaturation: A Method to Rank Slow Binding, High-Affinity **P38**.alpha. MAP Kinase Inhibitors
AU Kroe, Rachel R.; Regan, John; Proto, Al; Peet, Gregory W.; Roy, Tapon; Landro, Laura D.; Fuschetto, Natalie G.; Pargellis, Christopher A.; Ingraham, Richard H.
CS Department of Immunology and Inflammation, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, 06877, USA
SO Journal of Medicinal Chemistry (2003), 46(22), 4669-4675
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB It has been reported that the diaryl urea class of **p38**.alpha. inhibitors binds to **p38** map kinase with both high affinity and slow binding kinetics (Pargellis et al. Nat. Struct. Biol. 2002, 9, 268-272). The slow binding kinetics of this class of inhibitors is believed to be the result of binding to an allosteric pocket adjacent to the **p38**.alpha. active site. The use of traditional kinetic and equilibrium methods to measure the binding affinity of this class of compds. has created many challenges for determination of structure-activity relationships (SAR). The thermal denaturation method provides a means of measuring high-affinity interactions. In this paper, the method of thermal denaturation will be described as it has been applied to the diaryl urea class of **p38** map kinase inhibitors.
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 92 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:738968 HCAPLUS
DN 139:358017
TI Kinases, Homology Models, and High Throughput Docking

AU Diller, David J.; Li, Rixin
CS Pharmacopeia, Inc., Princeton, NJ, 08543-5350, USA
SO Journal of Medicinal Chemistry (2003), 46(22), 4638-4647
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB With the many protein sequences coming from the genome sequencing projects, it is unlikely that the authors will ever have an atomic resolution structure of every relevant protein. With high throughput crystallog., however, the authors will soon have representative structures for the vast majority of protein families. Thus the drug discovery and design process will rely heavily on protein modeling to address issues such as designing combinatorial libraries for an entire class of targets and engineering genome-wide selectivity over a target class. In this study the authors assess the value of high throughput docking into homol. models. To do this the authors dock a database of random compds. seeded with known inhibitors into homol. models of six different kinases. In five of the six cases the known inhibitors were enriched by factors of 4-5 in the top 5% of the overall scored and ranked compds. Furthermore, in the same five cases the known inhibitors were enriched by factors of 2-3 in the top 5% of the scored and ranked known kinase inhibitors, thus showing that the homol. models can pick up some of the crucial selectivity information.
RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 93 OF 119 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2003:281517 BIOSIS
DN PREV200300281517
TI Inhibition of coagulation, fibrinolysis, and endothelial cell activation by a **p38** mitogen-activated protein kinase inhibitor during human endotoxemia.
AU Branger, Judith [Reprint Author]; van den Blink, Bernt; Weijer, Sebastiaan; Gupta, Abhya; van Deventer, Sander J. H.; Hack, C. Erik; Peppelenbosch, Maikel P.; van der Poll, Tom
CS Laboratory of Experimental Internal Medicine, Academic Medical Center, University of Amsterdam, Meibergdreef 9, Room G2-105, 1105 AZ, Amsterdam, Netherlands
j.branger@amc.uva.nl
SO Blood, (June 1 2003) Vol. 101, No. 11, pp. 4446-4448. print.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Article
LA English
ED Entered STN: 19 Jun 2003
Last Updated on STN: 1 Aug 2003
AB **P38** mitogen-activated protein kinase (MAPK) is an important component of intracellular signaling cascades that initiate various inflammatory cellular responses. To determine the role of **p38** MAPK in the procoagulant response to lipopolysaccharide (LPS), 24 healthy subjects were exposed to an intravenous dose of LPS (4 ng/kg), preceded 3 hours earlier by orally administered 600 or 50 mg BIRB 796 BS (a specific **p38** MAPK inhibitor), or placebo. The 600-mg dose of BIRB 796 BS strongly inhibited LPS-induced coagulation activation, as measured by plasma concentrations of the prothrombin fragment F1 + 2. BIRB 796 BS also dose dependently attenuated the activation and subsequent inhibition of the fibrinolytic system (plasma tissue-type plasminogen activator, plasmin-alpha2-antiplasmin complexes, and plasminogen activator inhibitor type 1) and endothelial cell activation (plasma soluble E-selectin and von Willebrand factor). Activation of **p38** MAPK plays an important role in the procoagulant and endothelial cell response after in vivo exposure to LPS.

L17 ANSWER 94 OF 119 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 11
AN 2003:563239 BIOSIS
DN PREV200300564401
TI The kinetics of binding to **p38** MAP kinase by analogues of BIRB

796.

AU Regan, John [Reprint Author]; Pargellis, Christopher A.; Cirillo, Pier F.; Gilmore, Thomas; Hickey, Eugene R.; Peet, Gregory W.; Proto, Alfred; Swinamer, Alan; Moss, Neil

CS Departments of Medicinal Chemistry, Boehringer Ingelheim Pharmaceuticals, 900 Ridgebury Road, Ridgefield, CT, 06877, USA
jregan@rdg.boehringer-ingelheim.com

SO Bioorganic & Medicinal Chemistry Letters, (15 September 2003) Vol. 13, No. 18, pp. 3101-3104. print.
CODEN: BMCLE8. ISSN: 0960-894X.
DT Article
LA English
ED Entered STN: 3 Dec 2003
Last Updated on STN: 3 Dec 2003

AB BIRB 796, a member of the N-pyrazole-N'-naphthly urea class of **p38** MAPK inhibitors, binds to the kinase with both slow association and dissociation rates. Prior to binding, the kinase undergoes a reorganization of the activation loop exposing a critical binding domain. We demonstrate that, independent of the loop movement, association rates are governed by low energy conformations of the inhibitor and polar functionality on the tolyl ring. As anticipated, the dissociation rates of the inhibitors from the kinase are slowed by lipophilic and hydrogen bond interactions. The value of structure-kinetic relationships (SKR) in drug design is discussed.

L17 ANSWER 95 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:888719 HCAPLUS
DN 137:384854

TI Preparation of diaryl ureas as antiinflammatory agents

IN Cirillo, Pier F.; Goldberg, Daniel R.; Hammach, Abdelhakim; Moss, Neil; Regan, John Robinson

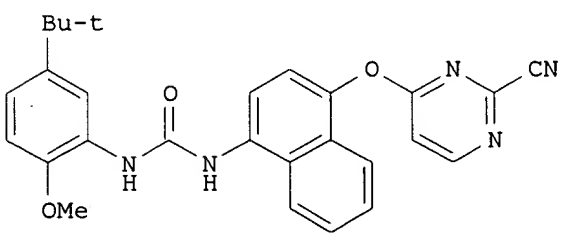
PA Boehringer Ingelheim Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002092576	A1	20021121	WO 2002-US14733	20020508
	W: AE, AU, BG, BR, CA, CN, CO, CZ, EC, EE, HR, HU, ID, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	CA 2445003	AA	20021121	CA 2002-2445003	20020508
	EP 1392661	A1	20040303	EP 2002-734324	20020508
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
	JP 2004530690	T2	20041007	JP 2002-589462	20020508
	US 2003008868	A1	20030109	US 2002-143322	20020510
	US 6852717	B2	20050208		
PRAI	US 2001-291425P	P	20010516		
	WO 2002-US14733	W	20020508		

GI



I

AB The title diaryl ureas, useful in pharmaceutic compns. for treating a cytokine mediated diseases or conditions involving inflammation such as chronic inflammatory diseases, were prepared Thus, treating 4-(2-chloropyrimidin-4-yloxy)naphthalen-1-ylamine with Et3N in DMF followed by addition of Et4NCN, and treatment of the resulting nitrile with phosgene, and reacting the intermediate with 5-tert-butyl-o-anisidine afforded the urea I.

L17 ANSWER 96 OF 119 USPATFULL on STN
AN 2002:157650 USPATFULL
TI Compounds useful as anti-inflammatory agents
IN Betageri, Rajashehar, Bethel, CT, UNITED STATES
Breitfelder, Steffen, Danbury, CT, UNITED STATES
Cirillo, Pier F., Woodbury, CT, UNITED STATES
Gilmore, Thomas A., Middlebury, CT, UNITED STATES
Hickey, Eugene R., Danbury, CT, UNITED STATES
Kirrane, Thomas M., JR., Danbury, CT, UNITED STATES
Moriak, Monica H., Danbury, CT, UNITED STATES
Moss, Neil, Ridgefield, CT, UNITED STATES
Patel, Usha R., Brookfield, CT, UNITED STATES
Proudfoot, John R., Newtown, CT, UNITED STATES
Regan, John R., Larchmont, NY, UNITED STATES
Sharma, Rajiv, Ridgefield, CT, UNITED STATES
Sun, Sanxing, Danbury, CT, UNITED STATES
Swinamer, Alan D., Danbury, CT, UNITED STATES
Takahashi, Hidenori, LaGrangeville, NY, UNITED STATES
PI US 2002082256 A1 20020627
US 6656933 B2 20031202
AI US 2001-962057 A1 20010925 (9)
RLI Division of Ser. No. US 2000-505582, filed on 16 Feb 2000, PENDING
PRAI US 1999-124148P 19990312 (60)
US 1999-165867P 19991116 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 6137
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel aromatic compounds which are useful for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are pharmaceutical compositions containing and processes of making such compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 97 OF 119 USPATFULL on STN
AN 2002:126768 USPATFULL
TI Aromatic heterocyclic compounds as antiinflammatory agents
IN Hickey, Eugene R., Danbury, CT, UNITED STATES
Regan, John R., Larchmont, NY, UNITED STATES
PI US 2002065285 A1 20020530
US 6506748 B2 20030114
AI US 2001-891820 A1 20010626 (9)
RLI Division of Ser. No. US 2000-484638, filed on 18 Jan 2000, PENDING
PRAI US 1999-116400P 19990119 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2251
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are novel aromatic heterocyclic compounds of the formula(I) wherein Ar.sub.1,Ar.sub.2,L,Q and X are described herein. The compounds are useful in pharmaceutic compositions for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are processes of making such compounds. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 98 OF 119 USPATFULL on STN
AN 2002:112936 USPATFULL
TI Aromatic heterocyclic compounds as antiinflammatory agents
IN Cirillo, Pier F., Woodbury, CT, UNITED STATES
Gilmore, Thomas A., Middlebury, CT, UNITED STATES
Hickey, Eugene R., Danbury, CT, UNITED STATES
Regan, John R., Larchmont, NY, UNITED STATES
Zhang, Lin-Hua, New Fairfield, CT, UNITED STATES
PI US 2002058678 A1 20020516
AI US 2001-879776 A1 20010612 (9)
RLI Division of Ser. No. US 2000-484638, filed on 18 Jan 2000, PENDING
PRAI US 1999-116400P 19990119 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P.O. BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2275
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel aromatic heterocyclic compounds of the formula(I) wherein Ar.sub.1, Ar.sub.2, L, Q and X are described herein. The compounds are useful in pharmaceutic compositions for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are processes of making such compounds. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 99 OF 119 USPATFULL on STN
AN 2002:106298 USPATFULL
TI Compounds useful as anti-inflammatory agents
IN Betageri, Rajashehar, Bethel, CT, UNITED STATES
Breitfelder, Steffen, Danbury, CT, UNITED STATES
Cirillo, Pier F., Woodbury, CT, UNITED STATES
Gilmore, Thomas A., Middlebury, CT, UNITED STATES
Hickey, Eugene R., Danbury, CT, UNITED STATES
Kirrane, Thomas M., Danbury, CT, UNITED STATES
Moriak, Monica H., Danbury, CT, UNITED STATES
Moss, Neil, Ridgefield, CT, UNITED STATES
Patel, Usha R., Brookfield, CT, UNITED STATES
Proudfoot, John R., Newtown, CT, UNITED STATES
Regan, John R., Larchmont, NY, UNITED STATES
Sharma, Rajiv, Ridgefield, CT, UNITED STATES
Sun, Sanxing, Danbury, CT, UNITED STATES
Swinamer, Alan D., Danbury, CT, UNITED STATES
Takahashi, Hidenori, LaGrangeville, NY, UNITED STATES
PI US 2002055507 A1 20020509
US 6660732 B2 20031209
AI US 2001-962709 A1 20010925 (9)
RLI Division of Ser. No. US 2000-505582, filed on 16 Feb 2000, PENDING
PRAI US 1999-124148P 19990312 (60)
US 1999-165867P 19991116 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 22

ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 6968
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel aromatic compounds which are useful for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are pharmaceutical compositions containing and processes of making such compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 100 OF 119 USPATFULL on STN
AN 2002:54385 USPATFULL
TI Oral dosage formulations of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl] urea
IN Cappola, Michael, Wilton, CT, UNITED STATES
Gereg, George W., Bethel, CT, UNITED STATES
Way, Susan, Danbury, CT, UNITED STATES
PI US 2002031544 A1 20020314
US 6565880 B2 20030520
AI US 2001-902822 A1 20010711 (9)
PRAI US 2000-220387P 20000724 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 681
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A formulation comprising, and process for preparing, improved oral dosage forms of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea, a chemical entity with anti-inflammatory properties. Granulation of 1-(5-tert-but 1-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea within specified ranges provides improved dissolution of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea and oral bioavailability, as well as content uniformity. Incorporation into the formulation of an aqueous soluble inclusion compound capable of forming a complex with 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea, such as beta-cyclodextrin provides enhanced stability of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea, in particular in highly ionic environments. Chipping and disintegration of tablets containing more than about 10% betacyclodextrin can be prevented by applying a polymeric coat to the surface of the tablet at a temperature below 40° C.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 101 OF 119 USPATFULL on STN
AN 2002:326126 USPATFULL
TI Bis pyrazole-1H-pyrazole intermediates and their synthesis
IN Kapadia, Suresh R., Danbury, CT, United States
Song, Jinhua J., Hopewell Junction, NY, United States
Yee, Nathan K., Danbury, CT, United States
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)
PI US 6492529 B1 20021210
AI US 2002-67492 20020205 (10)
RLI Continuation-in-part of Ser. No. US 2001-920899, filed on 2 Aug 2001, now patented, Pat. No. US 6372773 Division of Ser. No. US 2000-484638, filed on 18 Jan 2000, now patented, Pat. No. US 6319921
DT Utility
FS GRANTED
EXNAM Primary Examiner: Ramsuer, Robert W.

LREP Raymond, Robert P., Bottino, Anthony P., Stempel, Alan R.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 2219
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are aromatic heterocyclic compounds of the formula (I) wherein Ar.sub.1, Ar.sub.2, L, Q and X are described herein, and intermediate compounds useful for making such compounds. The compounds are useful in pharmaceutic compositions for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. ##STR1##

Also disclosed are processes of making compounds of the formula (I), their intermediates and processes of making such intermediates, including bis pyrazole-1H-pyrazole intermediates of the formula: ##STR2##

wherein Alk, R.sub.x and R.sub.z are described herein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 102 OF 119 USPATFULL on STN
AN 2002:81512 USPATFULL
TI Aromatic heterocyclic compounds as antiinflammatory agents
IN Regan, John R., Larchmont, NY, United States
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)
PI US 6372773 B1 20020416
AI US 2001-920899 20010802 (9)
RLI Division of Ser. No. US 2001-891579, filed on 26 Jun 2001, now patented, Pat. No. US 6329415 Division of Ser. No. US 2000-484638, filed on 18 Jan 2000, now patented, Pat. No. US 6319921
PRAI US 1999-116400P 19990119 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Ramsuer, Robert W.
LREP Raymond, Robert P., Bottino, Anthony P., Stempel, Alan R.
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 2201
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel aromatic heterocyclic compounds of the formula(I) wherein Ar.sub.1,Ar.sub.2,L,Q and X are described herein. The compounds are useful in pharmaceutic compositions for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are processes of making such compounds. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 103 OF 119 USPATFULL on STN
AN 2002:57780 USPATFULL
TI Compounds useful as anti-inflammatory agents
IN Breitfelder, Steffen, Danbury, CT, United States
Cirillo, Pier F., Woodbury, CT, United States
Gilmore, Thomas A., Middlebury, CT, United States
Hickey, Eugene R., Danbury, CT, United States
Proudfoot, John R., Newtown, CT, United States
Regan, John R., Larchmont, NY, United States
Swinamer, Alan D., Danbury, CT, United States
Takahashi, Hidenori, LaGrangeville, NY, United States
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)
PI US 6358945 B1 20020319
AI US 2000-505582 20000216 (9)
PRAI US 1999-124148P 19990312 (60)

US 1999-165867P 19991116 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Raymond, Richard L.
LREP Raymond, Robert P., Bottino, Anthony P., Stempel, Alan R.
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 6875
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel aromatic compounds which are useful for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are pharmaceutical compositions containing and processes of making such compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 104 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:289124 HCAPLUS
DN 137:179568
TI Anti-inflammatory effects of a **p38** mitogen-activated protein kinase inhibitor during human endotoxemia
AU Branger, Judith; Van den Blink, Bernt; Weijer, Sebastiaan; Madwed, Jeffrey; Bos, Carina L.; Gupta, Abhya; Yong, Chan-Loi; Polmar, Stephen H.; Olszyna, Dariusz P.; Hack, C. Erik; Van Deventer, Sander J. H.; Peppelenbosch, Maikel P.; Van der Poll, Tom
CS Laboratory of Experimental Internal Medicine and Department of Infectious Diseases, Tropical Medicine, Academic Medical Center, University of Amsterdam, Amsterdam, 1105 AZ, Neth.
SO Journal of Immunology (2002), 168(8), 4070-4077
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB The **p38** mitogen-activated protein kinase (MAPK) participates in intracellular signaling cascades resulting in inflammatory responses. Therefore, inhibition of the **p38** MAPK pathway may form the basis of a new strategy for treatment of inflammatory diseases. However, **p38** MAPK activation during systemic inflammation in humans has not yet been shown, and its functional significance in vivo remains unclear. Hence, we exposed 24 healthy male subjects to an i.v. dose of LPS (4 ng/kg), preceded 3 h earlier by orally administered 600 or 50 mg BIRB 796 BS (an in vitro **p38** MAPK inhibitor) or placebo. Both doses of BIRB 796 BS significantly inhibited LPS-induced **p38** MAPK activation in the leukocyte fraction of the volunteers. Cytokine production (TNF-α, IL-6, IL-10, and IL-1R antagonist) was strongly inhibited by both low and high dose **p38** MAPK inhibitor. In addition, **p38** MAPK inhibition diminished leukocyte responses, including neutrophilia, release of elastase-α1-antitrypsin complexes, and up-regulation of CD11b with down-regulation of L-selectin. Finally, blocking **p38** MAPK decreased C-reactive protein release. These data identify **p38** MAPK as a principal mediator of the inflammatory response to LPS in humans. Furthermore, the anti-inflammatory potential of an oral **p38** MAPK inhibitor in humans in vivo suggests that **p38** MAPK inhibitors may provide a new therapeutic option in the treatment of inflammatory diseases.
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 105 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:392357 HCAPLUS
DN 137:119059
TI Pyrazole Urea-Based Inhibitors of **p38** MAP Kinase: From Lead Compound to Clinical Candidate
AU Regan, John; Breitfelder, Steffen; Cirillo, Pier; Gilmore, Thomas; Graham, Anne G.; Hickey, Eugene; Klaus, Bernhard; Madwed, Jeffrey; Moriak, Monica; Moss, Neil; Pargellis, Chris; Pav, Sue; Proto, Alfred; Swinamer, Alan; Tong, Liang; Torcellini, Carol

CS Research and Development Center, Department of Medicinal Chemistry, Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, 06877, USA
SO Journal of Medicinal Chemistry (2002), 45(14), 2994-3008
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 137:119059
AB We report on a series of N-pyrazole, N'-aryl ureas and their mode of binding to **p38** mitogen activated protein kinase. Importantly, a key binding domain that is distinct from the ATP (ATP) binding site is exposed when the conserved activation loop, consisting in part of Asp168-Phe169-Gly170, adopts a conformation permitting lipophilic and hydrogen bonding interactions between this class of inhibitors and the protein. We describe the correlation of the structure-activity relationships and crystallog. structures of these inhibitors with **p38**. In addition, we incorporated another binding pharmacophore that forms a hydrogen bond at the ATP binding site. This modification affords significant improvements in binding, cellular, and in vivo potencies resulting in the selection of Compound 45 (BIRB 796) as a clin. candidate for the treatment of inflammatory diseases.
RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 106 OF 119 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2002:370687 BIOSIS
DN PREV200200370687
TI Pharmacological evaluation of BIRB 796, a selective inhibitor of **p38** map kinase (MAPK), in animal models of endotoxin shock, inflammation and arthritis.
AU Torcellini, Carol [Reprint author]; Zimmitti, Clare [Reprint author]; Weldon, Steven M. [Reprint author]; Nabozny, Gerald H. [Reprint author]; Jennewein, Michael [Reprint author]
CS Pharmacology, Boehringer Ingelheim Pharmaceuticals, Inc, 900 Ridgebury Road, POB 368, Ridgefield, CT, 06877, USA
SO FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1081. print.
Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.
CODEN: FAJOEC. ISSN: 0892-6638.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 3 Jul 2002
Last Updated on STN: 3 Jul 2002
AB BIRB 796, a selective **p38** MAPK inhibitor, was evaluated in a variety of inflammatory based animal models. In mice, BIRB 796, when orally administered 30-min prior to lipopolysaccharide (LPS) stimulation, inhibited TNFalpha production with an ED50 of apprx10 mg/kg. In cynomolgus monkeys, BIRB 796, when dosed IV at 1 and 3 mg/kg immediately prior to LPS stimulation, inhibited TNFalpha production by 90 and 94%. When administered orally 12-hr prior to LPS at 3 and 20 mg/kg, it inhibited TNFalpha production by 61% and 88%. BIRB 796 also inhibited LPS-stimulated neutrophil infiltration in rat bronchoalveolar lavage with an ED50 of apprx3 mg/kg, PO. In the collagen induced arthritis (CIA) model, mice treated with BIRB 796 at 30 mg/kg, QD (dosing began after the onset of the disease) displayed a reduction of arthritis progression by apprx70% versus vehicle controls over a 35-day treatment period. Thus, BIRB 796 is orally active, exhibits a potent and sustained inhibition of TNFalpha production and neutrophil infiltration, and protects against the progression of arthritis.

L17 ANSWER 107 OF 119 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 12
AN 2003:109920 BIOSIS
DN PREV200300109920
TI Inhibition of **p38** MAP kinase by utilizing a novel allosteric binding site.

AU Pargellis, Christopher [Reprint Author]; Tong, Liang; Churchill, Laurie; Cirillo, Pier F.; Gilmore, Thomas; Graham, Anne G.; Grob, Peter M.; Hickey, Eugene R.; Moss, Neil; Pav, Susan; Regan, John
CS Department of Biology, Research and Development Center, Boehringer Ingelheim Pharmaceuticals, 900 Ridgebury Road, Ridgefield, CT, 06877, USA cpargell@rdg.boehringer-ingelheim.com; tong@como.bio.columbia.edu
SO Nature Structural Biology, (April 2002) Vol. 9, No. 4, pp. 268-272. print. ISSN: 1072-8368 (ISSN print).
DT Article
LA English
ED Entered STN: 26 Feb 2003
Last Updated on STN: 26 Feb 2003
AB The **p38** MAP kinase plays a crucial role in regulating the production of proinflammatory cytokines, such as tumor necrosis factor and interleukin-1. Blocking this kinase may offer an effective therapy for treating many inflammatory diseases. Here we report a new allosteric binding site for a diaryl urea class of highly potent and selective inhibitors against human **p38** MAP kinase. The formation of this binding site requires a large conformational change not observed previously for any of the protein Ser/Thr kinases. This change is in the highly conserved Asp-Phe-Gly motif within the active site of the kinase. Solution studies demonstrate that this class of compounds has slow binding kinetics, consistent with the requirement for conformational change. Improving interactions in this allosteric pocket, as well as establishing binding interactions in the ATP pocket, enhanced the affinity of the inhibitors by 12,000-fold. One of the most potent compounds in this series, BIRB 796, has picomolar affinity for the kinase and low nanomolar inhibitory activity in cell culture.

L17 ANSWER 108 OF 119 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2002:511069 BIOSIS
DN PREV200200511069
TI Synthesis and biological evaluation of BIRB 796 analogs as potent inhibitors of **p38** MAP kinase.
AU Swinamer, Alan D. [Reprint author]; Capolino, Alison [Reprint author]; Cirillo, Pier F. [Reprint author]; Gilmore, Thomas [Reprint author]; Graham, Anne [Reprint author]; Hickey, Eugene [Reprint author]; Moriak, Monica [Reprint author]; Madwed, Jeff [Reprint author]; Moss, Neil [Reprint author]; Nelson, Richard [Reprint author]; Pargellis, Christopher [Reprint author]; Regan, John [Reprint author]; Torcellini, Carol [Reprint author]; Tsang, Michele [Reprint author]
CS Departments of Medicinal Chemistry, Biology and Pharmacology, Boehringer Ingelheim Pharmaceuticals, 900 Ridgebury Road, P. O. Box 368, Ridgefield, CT, 06877, USA
aswiname@rdg.boehringer-ingelheim.com
SO Abstracts of Papers American Chemical Society, (2002) Vol. 224, No. 1-2, pp. MEDI 303. print.
Meeting Info.: 224th National Meeting of the American Chemical Society. Boston, MA, USA. August 18-22, 2002.
CODEN: ACSRAL. ISSN: 0065-7727.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 2 Oct 2002
Last Updated on STN: 2 Oct 2002

L17 ANSWER 109 OF 119 USPATFULL on STN
AN 2001:200183 USPATFULL
TI Aromatic heterocyclic compounds and their use as anti-inflammatory agents
IN Regan, John R., Larchmont, NY, United States
Hickey, Eugene R., Danbury, CT, United States
Moss, Neil, Ridgefield, CT, United States
Cywin, Charles L., Bethel, CT, United States
Pargellis, Christopher, West Redding, CT, United States
Gilmore, Thomas A., Middlebury, CT, United States
PI US 2001039290 A1 20011108

PI US 6432995 B2 20020813
AI US 2001-808084 A1 20010314 (9)
RLI Division of Ser. No. US 1999-461446, filed on 14 Dec 1999, GRANTED, Pat. No. US 6228881 Division of Ser. No. US 1998-181743, filed on 29 Oct 1998, GRANTED, Pat. No. US 6080763
PRAI US 1997-64102P 19971103 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2147
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel aromatic heterocyclic compounds inhibit cytokines production involved in immunoregulation and inflammation such as interleukin-1 and tumor necrosis factor production. The compounds are therefore useful in pharmaceutic compositions for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 110 OF 119 USPATFULL on STN
AN 2001:235250 USPATFULL
TI Method of treating cytokine mediated diseases or conditions
IN Cirillo, Pier F., Woodbury, CT, United States
Gilmore, Thomas A., Middlebury, CT, United States
Hickey, Eugene R., Danbury, CT, United States
Regan, John R., Larchmont, NY, United States
Zhang, Lin-Hua, New Fairfield, CT, United States
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)
PI US 6333325 B1 20011225
AI US 2001-871559 20010531 (9)
RLI Continuation of Ser. No. US 2000-484638, filed on 18 Jan 2000
PRAI US 1999-116400P 19990119 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Ramsuer, Robert W.
LREP Raymond, Robert P., Bottino, Anthony P., Stempel, Alan R.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2234
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel aromatic heterocyclic compounds of the formula(I) wherein Ar.sub.1,Ar.sub.2,L,Q and X are described herein. The compounds are useful in pharmaceutic compositions for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are processes of making such compounds. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 111 OF 119 USPATFULL on STN
AN 2001:226669 USPATFULL
TI Aromatic heterocyclic compounds as antiinflammatory agents
IN Cirillo, Pier F., Woodbury, CT, United States
Regan, John R., Larchmont, NY, United States
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)
PI US 6329415 B1 20011211
AI US 2001-891579 20010626 (9)
RLI Division of Ser. No. US 2000-484638, filed on 18 Jan 2000
PRAI US 1999-116400P 19990101 (60)
DT Utility
FS GRANTED

EXNAM Primary Examiner: Ramsuer, Robert W.
LREP Raymond, Robert P., Bottino, Anthony P., Stempel, Alan R.
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2204
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel aromatic heterocyclic compounds of the formula(I) wherein Ar.sub.1,Ar.sub.2,L,Q and X are described herein. The compounds are useful in pharmaceutic compositions for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are processes of making such compounds. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 112 OF 119 USPATFULL on STN
AN 2001:208887 USPATFULL
TI Aromatic heterocyclic compound as antiinflammatory agents
IN Cirillo, Pier F., Woodbury, CT, United States
Gilmore, Thomas A., Middlebury, CT, United States
Hickey, Eugene R., Danbury, CT, United States
Regan, John R., Larchmont, NY, United States
Zhang, Lin-Hua, New Fairfield, CT, United States
PA Boerhinger Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)
PI US 6319921 B1 20011120
AI US 2000-484638 20000118 (9)
PRAI US 1999-116400P 19990119 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Ramsuer, Robert W.
LREP Raymond, Robert P., Bottino, Anthony P., Stempel, Alan R.
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2297
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel aromatic heterocyclic compounds of the formula (I) wherein Ar.sub.1, Ar.sub.2, L, Q and X are described herein. The compounds are useful in pharmaceutic compositions for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are processes of making such compounds. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 113 OF 119 USPATFULL on STN
AN 2001:67692 USPATFULL
TI Aromatic heterocyclic compounds and their use as anti-inflammatory agents
IN Regan, John R., Larchmont, NY, United States
Cirillo, Pier F., Woodbury, CT, United States
Hickey, Eugene R., Danbury, CT, United States
Moss, Neil, Ridgefield, CT, United States
Cywin, Charles L., Bethel, CT, United States
Pargellis, Christopher, West Redding, CT, United States
Gilmore, Thomas A., Middlebury, CT, United States
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)
PI US 6228881 B1 20010508
AI US 1999-461446 19991214 (9)
RLI Division of Ser. No. US 1998-181743, filed on 29 Oct 1998
PRAI US 1997-64102P 19971103 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Owens, Amelia
LREP Raymond, Robert P., Bottino, Anthony P., Stempel, Alan R.

CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2086
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel aromatic heterocyclic compounds inhibit cytokines production involved in immunoregulation and inflammation such as interleukin-1 and tumor necrosis factor production. The compounds are therefore useful in pharmaceutic compositions for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 114 OF 119 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2001:511075 BIOSIS
DN PREV200100511075
TI Pharmacological evaluation of BIRB 796, a selective inhibitor of **P38** MAP kinase (MAPK), in animal models of endotoxic shock, inflammation and arthritis.
AU Madwed, J. B. [Reprint author]; Torcellini, C. [Reprint author]; Weldon, S. M. [Reprint author]; Zimmitti, C. [Reprint author]; Nabozny, G. H. [Reprint author]; Souza, D. [Reprint author]; Raymond, E. [Reprint author]; Jennewein, M. [Reprint author]; Pargellis, C. [Reprint author]; Regan, J. [Reprint author]
CS Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, 06877, USA
SO Inflammation Research, (September, 2001) Vol. 50, No. Supplement 3, pp. S184. print.
Meeting Info.: 5th World Congress on Inflammation. Edinburgh, Scotland. September 22-26, 2001.
ISSN: 1023-3830.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 31 Oct 2001
Last Updated on STN: 23 Feb 2002

L17 ANSWER 115 OF 119 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2001:511043 BIOSIS
DN PREV200100511043
TI A novel series of **p38** MAP kinase inhibitors: Development of a clinical candidate, BIRB0796.
AU Pargellis, C. [Reprint author]; Tong, L. [Reprint author]; Madwed, J. [Reprint author]; Schwartz, R. [Reprint author]; Proto, A. [Reprint author]; Basso, M. [Reprint author]; Grob, P. [Reprint author]; Cirillo, P. [Reprint author]; Hickey, E. [Reprint author]; Gilmore, T. [Reprint author]; Moss, N. [Reprint author]; Regan, J. [Reprint author]
CS Boehringer Ingelheim Pharmaceuticals Inc., 900 Ridgebury Rd., Ridgefield, CT, 06877, USA
SO Inflammation Research, (September, 2001) Vol. 50, No. Supplement 3, pp. S149. print.
Meeting Info.: 5th World Congress on Inflammation. Edinburgh, Scotland. September 22-26, 2001.
ISSN: 1023-3830.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 31 Oct 2001
Last Updated on STN: 23 Feb 2002

L17 ANSWER 116 OF 119 USPATFULL on STN
AN 2000:80771 USPATFULL
TI Aromatic heterocyclic compounds and their use as anti-inflammatory agents
IN Regan, John R., Larchmont, NY, United States
Cirillo, Pier F., Woodbury, CT, United States
Hickey, Eugene R., Danbury, CT, United States

Moss, Neil, Ridgefield, CT, United States
Cywin, Charles L., Bethel, CT, United States
Pargellis, Christopher, West Redding, CT, United States
Gilmore, Thomas A., Middlebury, CT, United States
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)
PI US 6080763 20000627
AI US 1998-181743 19981029 (9)
PRAI US 1997-64102P 19971103 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Owens, Amelia
LREP Raymond, Robert P., Bottino, Anthony P., Stempel, Alan R.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2027
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel aromatic heterocyclic compounds inhibit cytokines production involved in immunoregulation and inflammation such as interleukin-1 and tumor necrosis factor production. The compounds are therefore useful in pharmaceutic compositions for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 117 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:619239 HCAPLUS
DN 133:344173
TI 1-Phenyl-5-pyrazolyl ureas: potent and selective **p38** kinase inhibitors
AU Dumas, J.; Hatoum-Mokdad, H.; Sibley, R.; Riedl, B.; Scott, W. J.; Monahan, M. K.; Lowinger, T. B.; Brennan, C.; Natero, R.; Turner, T.; Johnson, J. S.; Schoenleber, R.; Bhargava, A.; Wilhelm, S. M.; Housley, T. J.; Ranges, G. E.; Shrikhande, A.
CS Department of Chemistry Research, Bayer Research Center, West Haven, CT, 06516, USA
SO Bioorganic & Medicinal Chemistry Letters (2000), 10(18), 2051-2054
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Inhibitors of the MAP kinase **p38** are potentially useful for the treatment of arthritis and **osteoporosis**. Several 2,3-dichlorophenyl ureas were identified as small-mol. inhibitors of **p38** by a combinatorial chemical effort. Optimization for cellular potency led to the discovery of a new class of potent and selective **p38** kinase inhibitors, exemplified by the 1-phenyl-5-pyrazolyl urea 7 (IC50=13 nM).
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 118 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:425744 HCAPLUS
DN 131:73649
TI Preparation of pyrazolyl aryl ureas and related compounds as **p38** kinase inhibitors
IN Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Redman, Aniko; Sibley, Robert
PA Bayer Corporation, USA
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 9932110 A1 19990701 WO 1998-US26079 19981222
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2315647 AA 19990701 CA 1998-2315647 19981222
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
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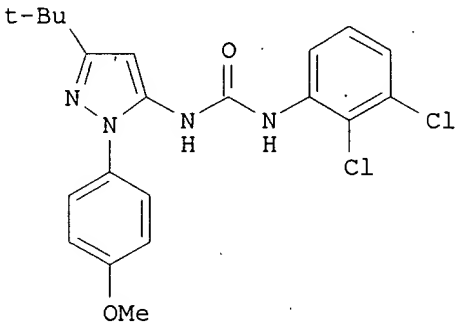

II

AB A method for treatment of **p38**-mediated disease other than cancer comprises administration of ANHCONHB [I; A = substituted pyrazolyl, thienyl, furyl; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl containing ≥1 5-6 membered aromatic structure containing 0-4 N, O, or S atoms]. Reaction of 2,3-dichlorophenyl isocyanate with 1-(4-methoxyphenyl)-3-tert-butyl-5-aminopyrazole in toluene gave title compound II. In an in vitro **p38** kinase assay, I displayed IC50 values of 1-10 μM.
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 119 OF 119 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:311199 HCAPLUS
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TI Preparation of aromatic heterocyclic compounds as antiinflammatory agents
IN Regan, John R.; Cirillo, Pier F.; Hickey, Eugene R.; Moss, Neil; Cywin, Charles L.; Pargellis, Christopher; Gilmore, Thomas A.
PA Boehringer Ingelheim Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
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OS MARPAT 130:325145

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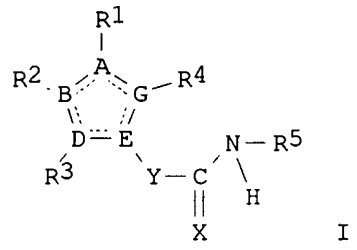

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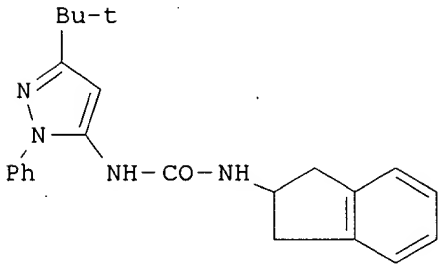

II

AB The title compds. I [A = C, N; B = C, N, O, etc.; D = C, N, S; E = C, N; G = C, S, N; X = S, O, etc.; Y = NH, etc.; R1 = (un)substituted, (partially or fully halogenated) alkyl, etc.; R2 is H, (partially or fully halogenated) alkyl, etc., when B is C or N; R3 is Ph, naphthyl, etc., when D is C or N; or R1R2 = fused Ph or pyridinyl ring; or R2R3 = fused Ph or pyridinyl ring; R4 is H, (partially or fully halogenated) alkyl when G is C or N; R5 is Ph, naphthyl, heteroaryl, etc.] are prepared I inhibit production of cytokines involved in immunoregulation and inflammation such as interleukin-1 and tumor necrosis factor. Pyrazole derivative II was prepared from phenylhydrazine and 4,4-dimethyl-3-oxopentanenitrile. Compds. of this invention had IC50 < 10 μM against TNF production in an in vitro assay using THP cells.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT